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LABORATORY AIDS IN THE DIAGNOSIS OF RENAL DISEASE

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IN DISCUSSING laboratory aids in the diagnosis of renal disease, the term "diagnosis" will be interpreted rather liberally to include the assessment of the degree, as well as the type, of kidney damage. Laboratory tests increase the clinician's ability to visualize and to follow the changes occurring in disease. Taken by themselves, such tests are usually of little use because similar results may have vastly different significances under different circumstances and it is only when interpreted by the physician in relation to his other findings that they are of real value. One should know, therefore, precisely what information each test will give and understand fully its limitations and possible fallacies.

The simplest and, in many cases, the only laboratory tests absolutely essential for diagnosis of renal disease are part of the urine analysis carried out by the physician. The detection of protein in the urine, the establishment of the presence or absence of hematuria or pyuria, along with a rough estimate of the numbers of red cells and pus cells in the urine, and the types of casts seen in the urine frequently give all the additional information necessary to confirm a diagnosis already suggested by the history and physical examination.

In such cases, further laboratory investigation is frequently desirable to establish the severity of the lesion and to follow its progress. There are, however, cases in which either the lesion is so slight that symptoms are absent or indefinite, or, occasionally, conditions are such that no proper history is obtainable, and in these, the diagnosis can be established only with the aid of, *not by*, further laboratory tests.

The significance of laboratory tests may be discussed from two aspects: (*a*) the information which they give as to the condition of the organs or functions being studied and (*b*) their use in the diagnosis of disease. As this latter aspect falls properly within the purview of clinical studies the present discussion will be confined to the former and will deal with only the procedures of the chemical laboratory.

When the kidney is damaged, the effects may be manifested by the appearance of abnormal constituents in the urine, by impairment of renal function or, more frequently, by both.

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ABNORMAL CONSTITUENTS

The methods for detecting the abnormal constituents which appear in the urine in renal disease are described fully in the *Instructions For The Laboratory Course In Pathological Chemistry* and in all standard works on clinical laboratory methods. These abnormal constituents are protein (albumin), hemoglobin (usually in red cells), pus cells, renal epithelial cells and casts.

PROTEINURIA (ALBUMINURIA)

Not Due To Renal Disease

The finding of protein in the urine in amounts which are detectable by the routine tests commonly employed is usually evidence of increased permeability of the glomerular membranes. With few exceptions (for example, Bence-Jones protein and the albumin appearing in the urine after the ingestion of large quantities of raw egg white), the proteins appearing in the urine are normal serum albumin and globulins and, because of its smaller size, serum albumin accounts for the much larger fraction in all instances. Sudden changes in renal blood flow, renal anoxia and congestion of the renal vessels may result in temporary changes in glomerular permeability which allow the passage of serum proteins.

One may encounter albuminuria, therefore, after violent exercise, prolonged exposure to cold and in all disease conditions associated with severe dehydration or shock. It is also found in cases of myocardial failure with chronic passive congestion and following convulsions. In all these cases, the cause of the albuminuria is usually obvious and it is only if the patient is comatose and no history is available that there is any possibility of ascribing the albuminuria to renal disease.

There are, however, cases of so-called benign albuminuria which must be differentiated from latent renal disease. In these cases, painstaking microscopic searches of the urinary sediment and tests of renal function must be made to eliminate the possibility of renal disease. This type of albuminuria occurs in young individuals, the majority between the ages of eight and eighteen years, and has been found in about five percent of the population in this age group.

In addition, there are the cases of so-called orthostatic albuminuria in whom the urine passed when the patient is in the recumbent position contains no albumin but who show an increasing albuminuria when they are up and about. These individuals are usually tallish, poorly developed individuals and it is thought that the cause of the albuminuria lies in an abnormal mobility of the kidney, which Rytand (1) has demonstrated by X-ray studies, leading to compression of the ureters or renal vessels when the patient assumes the erect position. The periodicity of this albuminuria and its tendency to intensification following exercise or the assumption of a position of extreme lordosis, will rule out the possibility of renal disease, provided the microscopic examination of the urine reveals no abnormality and the tests of kidney function are satisfactory.

In all the types of albuminuria which are produced by causes other than actual renal disease, the changes in glomerular permeability are relatively slight. The protein consists almost entirely of albumin and the amount of protein present, except at the height of an orthostatic albuminuria, is relatively small.

Due To Renal Disease

The proteinuria of renal disease is the result of inflammatory damage to the glomeruli, acute, subacute or chronic, and is always accompanied, at least periodically, by microscopic findings in the urine indicating an inflammatory lesion in the kidney and, in most cases, by evidences of impaired kidney function.

The amount of protein in the urine in renal disease will depend on two factors (*a*) the amount by which lesion in the glomerulus increases its permeability, that is, the degree to which the size of the pores in the glomerular membranes are increased, and (*b*) the amount of blood flowing through the glomeruli. Because of the interaction of these two factors, the amount of protein in the urine gives no indication of the severity of the renal lesion. In acute glomerulonephritis, for instance, there may be a much heavier albuminuria in a mild case with most of the glomerular loops still open than in a very severe case where most of the glomerular capillaries are closed by epithelial cell proliferation. In chronic glomerulonephritis, the heaviest proteinuria occurs in cases of the nephrotic syndrome where the glomerular damage may be relatively slight, as evidenced by the facts that little protein other than albumin appears in the urine and that tests of kidney function frequently show relatively little diminution in the amount of glomerular filtrate; whereas, in the more advanced stages of chronic nephritis, where the glomerular membrane is damaged to such an extent that it will let through the larger globulin molecules, the amount of proteinuria may be relatively small because the total amount of filtrate is greatly reduced.

These effects may be illustrated by two hypothetical cases. Let us suppose that a case of the nephrotic syndrome with a practically normal rate of glomerular filtration (that is, 170 litres per day) is excreting 1000 ml. of urine containing 3% of protein in the twenty-four hours, a loss of 30 grams of protein per day. The concentration of protein in the glomerular filtrate in such a case would be $30 \times 100/170{,}000 = 0.0174$ gms. or 17.4 mgms. per cent.

In the case of an individual with the rate of glomerular filtration cut to 20 litres per day and a twenty-four hour urine output of 2500 ml. containing 0.4% of protein, a loss of 10 grams per day, the glomerular filtrate would contain $10 \times 100/20{,}000 = 0.050$ gms. or 50.0 mgms. per cent, nearly three times the concentration in the first case which lost three times as much protein in the twenty-four hours and which had a urinary protein concentration of over seven times that of the second case. The relative proportions of albumin and globulin in the urine, however, do give some indication of the degree of glomerular damage. In the nephrotic syndrome, the ratio of albumin to globulin in the urine is 1:10. The proportion of globulin increases with increasing hyalinization of the glomeruli until in advanced chronic glomerulonephritis, the ratio has dropped to below 5:1. Although the determination of the A/G ratio of the urinary protein is not used for clinical purposes, a knowledge of these facts helps one to understand why progressive glomerular damage is usually associated with a decreasing concentration of protein in the urine.

HEMATURIA

The presence of red cells in the sediment from a centrifuged specimen of urine in numbers greater than one or two

per high power field is nearly always evidence of a lesion in the urinary tract and, if it has been ascertained by clinical observations that the blood cells are of renal origin, it is indicative of renal damage. It is true that some normal individuals may show up to 500,000 red blood cells in a twelve hour specimen but even this does not represent more than two to three red cells per high power field in a centrifuged specimen. The presence of more than this number of erythrocytes of renal origin in the urine is usually evidence of an active inflammatory process in the glomeruli. The number of cells varies with the intensity of the inflammatory reaction. In acute glomerulonephritis, or during an acute exacerbation of chronic nephritis, the hematuria may be so intense as to give the urine a dark reddish-brown colour; whereas, in latent chronic nephritis and in the advanced stages of it, the red cells may number only a few hundred thousand in the twenty-four hours.

CASTS

Casts are composed of coagulated protein either alone or containing cells or cellular debris. The type of cast varies with the type of renal lesion and the significance of casts may depend on their type, their numbers or both.

Hyaline Casts

Hyaline casts, in small numbers, may be found in the urine of normal individuals and, in moderately large numbers, in any of the extra-renal conditions causing proteinuria. In advanced chronic nephritis, they are present in considerable numbers at some times and are absent at others, having a tendency to occur in showers. They are also found in the healing stages of acute nephritis but disappear when the kidney is restored to normal.

They are of significance only when occurring in considerable numbers and as many as ten thousand may be found in the twelve-hour night urine of healthy individuals.

Granular Casts

Finely and coarsely granular casts are probably never found in normal urine, and their presence is indicative of renal damage. The matrix is the same as that of the hyaline casts and the granules are probably remnants of degenerated epithelial cells, red cells or pus cells. If the granules or casts have a brownish, orangish or yellowish appearance in a urine which contains no bile, they are undoubtedly remnants of red blood cells and are of a similar significance to the red cell casts about to be discussed. Granular casts are found in degenerative or inflammatory renal disease, in chronic passive congestion of the kidney due to myocardial failure, in severe dehydration and in surgical shock.

Red Cell Casts

Red cell casts are characteristic of glomerulonephritis, although they may be found in severe dehydration, particularly when alkalosis is present, and in surgical shock. With these exceptions, however, the finding of red cell casts, or the yellowish, orangish or brownish granular casts which indicate the presence of hemolysed red blood cells, is almost pathognomonic of a glomerulonephritis. At the height of an acute nephritis, red cell casts are usually numerous. They diminish in number as the lesion heals but, as long as any casts containing red cells or their remnants can be found, there is still an active glomerular lesion. It is essential, therefore, that the urine

(preferably the concentrated urine passed after a period of fluid restriction) of an individual who has had an acute nephritis should be examined repeatedly to make certain that no such casts are present. The same holds true in deciding whether an individual who has an albuminuria with no history or symptoms suggestive of renal disease is a case of latent chronic nephritis or of benign albuminuria. Careful and repeated searches of specimens of concentrated urine should be made and, if any casts containing red blood cells or red cell debris are found, it is almost certain that the case is one of latent chronic nephritis.

Epithelial Cell Casts

Epithelial cell casts occur in any condition in which degeneration of the tubular epithelium occurs. They are found in the nephrosis of metallic poisoning, many severe generalized infections and in the nephrotic stage of glomerulonephritis.

White Cell Casts

Leukocyte casts composed almost entirely of pus cells are usually found in pyelonephritis.

IMPAIRED RENAL FUNCTION

Although the diagnosis of renal disease usually may be made with the aid of the above routine procedures, there is a small group of cases in which tests to determine whether or not there is any diminution in kidney function are necessary to establish the diagnosis. It is also desirable to determine the changes in kidney function occurring in cases of established renal disease if the progress of the disease is to be followed intelligently.

There are two types of kidney function tests: (*a*) those which can be done with no equipment other than an accurate urinometer and a graduated cylinder to measure the urinary volume and (*b*) those which can be done only with the assistance of the chemical laboratory.

The tests of kidney function which can be performed simply by observations of the volume and specific gravity of the urine under certain specified conditions are based on the fact that the kidney, in the performance of its ordinary functions is called upon to excrete widely varying amounts and proportions of water, salts, urea and other end products of protein metabolism. To do this, the kidney must be able to vary the volume and specific gravity of the urine over a wide range. The capacity to vary the concentration of the urine is one of the most striking characteristics of the normal kidney and a reduction in this capacity, particularly in the ability to concentrate, is one of the earliest signs of decreased functional efficiency.

Both the concentrating power of the kidney, and its diluting power are greatly in excess of any ordinary requirement. It is possible, therefore, for either, or both, to undergo considerable diminution without any evident effect upon the volume, the specific gravity, or the composition of the urine. In such a state, the kidney, so long as it is not subjected to any unusual strain, performs its excretory functions as adequately as ever. Its subnormal capacity will be revealed only by tests which subject it to strain, or which, like the urea clearance test, measure its excretory performance against a normal standard.

THE TWO HOUR TEST

The simplest method of testing renal efficiency consists, in fact, in observing the fluctuations of urinary volume and specific gravity under the ordinary

conditions of everyday life. This is best accomplished by following the routine prescribed in the so-called "two-hour test," associated with the name of Mosenthal. In this routine, it is not now considered necessary to place the patient under any special restrictions with respect to food, drink, or activity, but it is desirable that no liquid be taken at night, that is, after 6 p.m. on the day before the test. The bladder is emptied just before breakfast, say at 8 a.m., and the first specimen of urine is collected exactly 2 hours later. Other specimens are taken every second hour thereafter up to the twelfth hour (8 p.m.). The urine passed during the remaining twelve hours of the twenty-four constitutes the "night urine," and is united into a single specimen. All seven specimens are measured, and the specific gravity of each is determined.

The response of normal kidneys to this routine presents the following features:

(*a*) At least one of the seven specimens shows a specific gravity of 1.020 or more.

(*b*) The difference between the maximum specific gravity observed and the lowest is at least 0.009.

(*c*) The night urine has a volume which does not exceed 725 cc.

The response of abnormal kidneys depends on the nature and degree of the renal damage. In acute nephritis or nephrosis, the volume of the excreted urine is diminished and its specific gravity raised. If recovery follows, the discharge of retained water leads to high urine volumes with low specific gravities. Under such circumstances, the test gives little information of value in either diagnosis or prognosis.

The chief usefulness of the two-hour test is in detecting, and following the course of chronic glomerulonephritis. In this condition, the first indications of defective function are a failure of the specific gravity to rise to 1.020 at any time, and a diminution in the range of its variations. These indications are usually accompanied by some increase in the volume of the night urine. As renal damage increases, the specific gravity continues to decrease, and its variability to diminish, until, finally, it becomes fixed at 1.009-1.011. At the same time, polyuria develops and increases, while the night volume rises to equal or surpass that of the day. In the final stages, the urine volume sinks again, but its specific gravity remains low.

The two-hour test tells us how successfully the kidney is meeting the demands actually being made upon it at the time. Apart from the fact that its indications are merely qualitative, its principal deficiencies are that (*a*) in the earlier stages of a progressive degeneration, it gives no information concerning the extent to which the reserve powers of the kidney have already been called into play, and (*b*) in the later stages, once the specific gravity has become fixed, it does not reveal the rate at which further deterioration is taking place.

THE CONCENTRATION TEST

The earliest function of the kidney to be impaired is its ability to do osmotic work and, as the production of an extremely concentrated urine places the greatest osmotic load on the kidney, it is this capacity which is first affected when the kidney is damaged. A reduction of total kidney substance, even when the remaining kidney tissue is quite normal, reduces the ability of the kidney to concentrate and, in renal disease, a relatively slight generalized lesion is made manifest by a reduction in concentrating power. This decrease in concentrating power has little effect

on the kidney's ability to excrete the total amount of the end products of protein metabolism produced during the twenty-four hours until there has been a very marked degree of kidney damage. The urea and other substances are simply excreted in an increasingly larger volume of fluid showing less and less variation in specific gravity until the stage is reached where there is little variation of urine flow from hour to hour and no variation whatsoever in the specific gravity. Even at this point, in some cases, there may be little retention of protein end products. At first, the only effect is a decrease in the kidneys' ability to respond to water deprivation by elaborating a urine of minimum volume for the amount of material to be excreted, that is, a urine of maximum specific gravity. This deficiency will not give rise to any symptoms at first because it is only the kidneys' ability to cope with conditions of physiological stress which has been affected. As the renal damage becomes greater, the kidneys will not be able to concentrate sufficiently to excrete the nitrogenous substances and salts in the usual volume of urine and there is some increase in the volume of night urine. With increasing renal damage, the sequence of events described in the discussion of the two hour test occurs.

There are several variations of the concentration test. The method described in the *Instructions For The Laboratory Course in Pathological Chemistry* has the advantage of being simple to apply and easily adapted for office practice. A normal individual will excrete a urine with a specific gravity of 1.025 or higher during the course of this test. A maximum specific gravity of 1.023, for example, is evidence of impairment of renal function provided that the test has been carried out properly and the subject has not been in the habit of taking excessive amounts of fluid and is not edematous.

In cases where the lowering of the maximum specific gravity is slight, or where more accurate assessment of the degree of renal damage is desired, the Lashmet-Newburgh concentration test should be done. The test is performed as follows:

After an evening meal the patient is instructed to take no fluids until the test has been completed. Solid food is not prohibited, but, if taken at all, must be restricted to items selected for their dryness—such articles, for example, as bread, dry cereals, butter, heavy cream, dried fruits, sugar, etc. All urine passed up to bed-time, the second night is discarded. A sample is collected the following morning, and its specific gravity is determined. Two hours later a second sample is obtained. If the specific gravity of this sample is no higher than that of the first, the test is terminated. Otherwise a third sample, and, if necessary, still others are collected at two hour intervals, until it is clear that the maximum specific gravity attainable by the patient has been reached.

A normal response is a maximum specific gravity of at least 1.029. Any maximum lower than this indicates a deficiency of concentrating power.

This test may be interpreted in a roughly quantitative manner in terms of the amount of renal damage in cases of chronic glomerulonephritis.

Alving and Van Slyke (1934) compared a number of concentration tests with the urea clearance test and found that over a considerable range there was a parallel decrease in the urea clearance and in the maximum specific gravity obtained by the Lashmet-Newburgh concentration

test. Correlation between the results of the urea clearance test and other concentration tests, though similar, was not so good as with the Lashmet-Newburgh test.

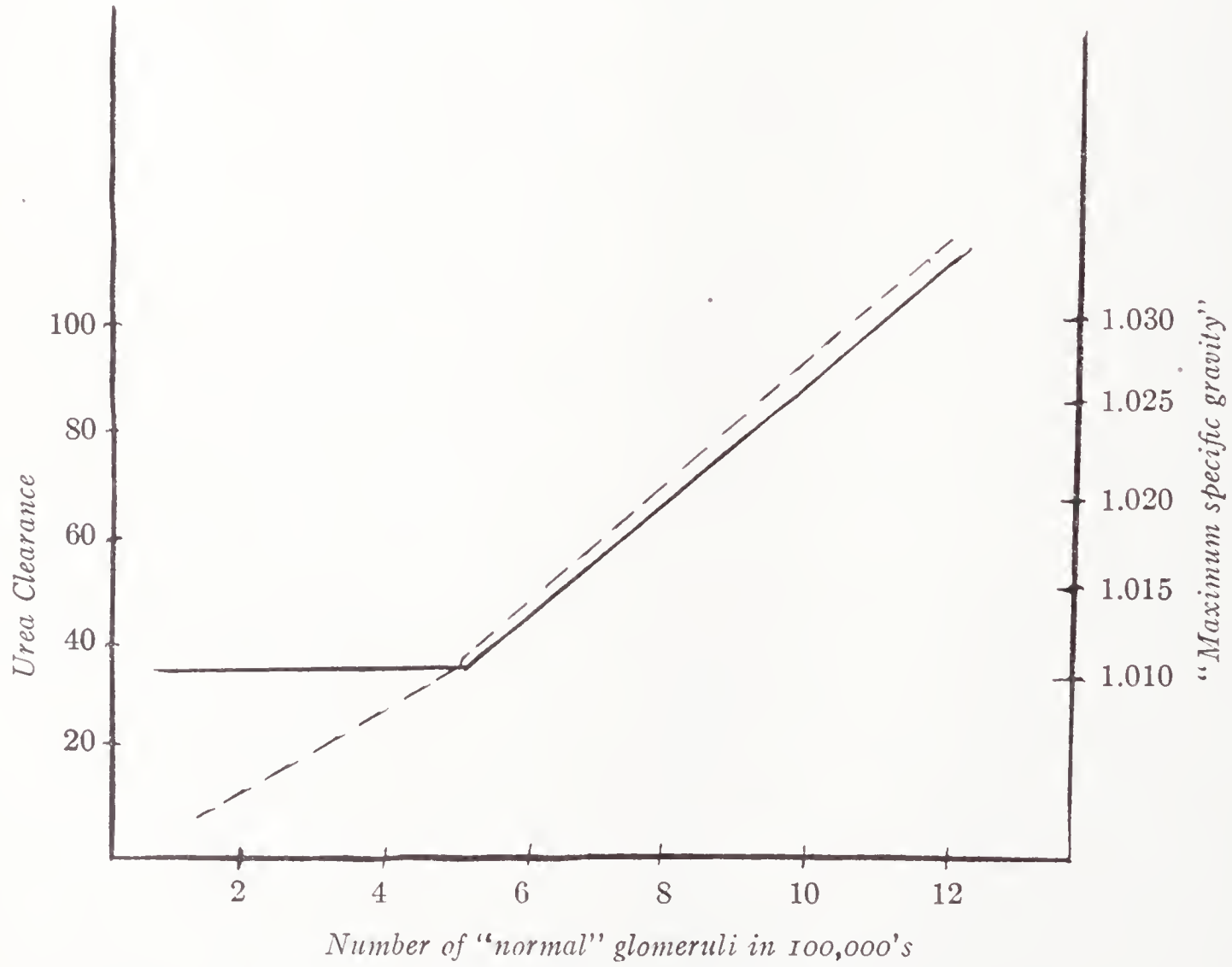
Later, Hayman and co-workers (1939) compared the results of the urea clearance test and the Lashmet-Newburgh concentration test done shortly before death with the number of glomeruli found in the kidneys obtained at autopsy. Then, they estimated the degree of damage in the glomeruli, and counted and charted the results in terms of the number of "normal" glomeruli—counting two glomeruli with an estimated fifty percent of the normal filtering surface, four glomeruli with an estimated twenty-five percent of the normal filtering surface or ten glomeruli with an estimated ten percent of the normal filtering surface as one "normal" glomerulus.

From the figures given by these two sets of authors, one can, for cases of chronic nephritis, obtain a rough idea of the amount of destruction of renal tissue which will result in a given maximum specific gravity or urea clearance.

Figure 1 is a graph based on the data of Alving and Van Slyke and of Hayman *et al.* giving the relation between the urea clearance, the maximum specific gravity obtained by the Lashmet-Newburgh test and the number of "normal" glomeruli in the kidney.

Using the figure of 1,200,000, the

FIGURE 1



Relation between the number of "normal" glomeruli, the "maximum specific gravity" and the urea clearance.

"Maximum specific gravity" ———— Urea Clearance - - - - - -

normal average number of glomeruli, as the basis for calculation, it can be seen that when the estimated amount of glomerular filtering surface is reduced to five-sixth there is a drop in the maximum specific gravity to about 1.027, yet the urea clearance remains well within the normal limits of from 75% to 125% of the average normal. It is not until the amount of glomerular filtering surface has been reduced to three-quarters of the normal amount and the average maximum specific gravity to 1.023 that the urea clearance drops beneath the lower limit of normal. From this point until the filtering surface has been reduced to one third of normal, the drops in maximum specific gravity and in urea clearance run parallel. The average maximum specific gravity is now 1.010 and the urea clearance about 25% of normal. Further renal damage produces no change in the maximum specific gravity. At this stage, there is a total loss of concentrating power so that the specific gravity of the urine is now the same as that of the glomerular filtrate, that is, of deproteinized plasma. In considering this relationship between the maximum specific gravity obtainable with the concentration test and the degree of renal damage, it must be remembered that it is only a rough approximation. In the first place, the specific gravities given are averages and in the second place, the estimation of the number of "normal" glomeruli is, at best, a rough one. Nevertheless, over the range in which comparisons can be made, the concentration test gives as accurate an estimate of renal damage as the more elaborate urea clearance test and it has the advantage of detecting minor degrees of renal inefficiency which are not revealed by any other means. In cases of mild latent glomerulonephritis, during recovery from acute nephritis and in some cases of vascular nephritis, the concentration test may give evidence of a slight diminution in kidney function which is not revealed by any other test.

It will have been noted that the decrease in maximum specific gravity has been related to a reduction in glomerular filtering surface whereas concentrating the urine is a tubular function. This correlation with diminution in glomeruli is made because it is impossible to assess the amount of tubular destruction in kidney sections and because it has been found that the reduction in tubular function follows fairly closely the amount of glomerular damage. In cases in which the damage is mostly tubular, for example, in mercuric chloride poisoning, in the shock kidney, or in the transfusion kidney, the degree of urine retention is usually so marked that the concentration test is contraindicated.

The limitations of the concentration test are: (*a*) It will give no information as to further deterioration in kidney function once fixation of specific gravity has taken place. (*b*) The test should not be performed if there is an increased blood non-protein-nitrogen or if there is a marked obligatory polyuria. In these cases, the performance of the concentration test may result in a marked increase in the azotemia or produce a dangerous degree of dehydration. (*c*) In patients with edema, the test is unreliable as the elimination of edema fluid, which may occur during, or even be initiated by, the procedure of the test, will, of course, result in the production of a urine of low specific gravity, not because of any lack of renal concentrating power but because the kidney must elaborate a dilute urine to excrete the

TABLE I

Constituent	Normal Limits	Normal Mean
Total Non-protein Nitrogen	23-42 mgms./100 cc.	32 mgms./100 cc.
Urea Nitrogen*	5-23	14
Urea*	11-48	29
Creatinine	1-2	1.5

*The lowest urea values are found only in women. For men, the minimum urea concentration is about 26 mgms. corresponding to about 12 mgms. of Urea Nitrogen.

excess fluid which is being poured into the blood from the extra-cellular spaces.

BLOOD ANALYSIS

The blood is usually examined in cases of renal disease to determine whether or not there has been any accumulation of the end products of protein metabolism. Retention of these substances occurs when there is a marked diminution in the blood flow through the glomeruli as is the case in acute glomerulonephritis, when the tubules are so damaged that they can no longer prevent the tubular urine from diffusing back through them into the blood—the situation which is found, for example, in mercuric chloride poisoning and in the lower nephron nephrosis which may follow traumatic shock or other conditions in which there is a prolonged period of renal anoxia, or when the number of effective kidney units has been so reduced that the resulting loss of concentrating power cannot be compensated for by polyuria, as occurs in advanced chronic nephritis.

The blood constituents most frequently determined in renal disease are urea, creatinine and total non-protein nitrogen. Normally these vary within the limits shown in Table I.

It does not matter much which of these substances is followed and the determination of the non-protein nitrogen will give as much information as any.

In Table II, is a comparison of the total non-protein nitrogen values with the results of the urea clearance test and the maximum specific gravity obtained by the concentration test.

It will be seen that, in a general way, the urea and total non-protein nitrogen levels increase with advancing impairment of renal function; but that (*a*) the increase is not conspicuous until the impairment has become really marked, and (*b*) even when the damage is severe,

TABLE II

Degree of Impairment	Urea Clearance Test	Non-protein Nitrogen	Maximum Specific Gravity
Very Slight	60%	23-42 mgm./100 cc.	1.020
Slight	40	30-50	1.015
Moderate	20	35-90	1.010
Severe	10	40-150	1.010
Very Severe	10	60-220	1.010
Uremia		up to 350	1.010

the increase, in individual cases, may be relatively small. However, once the stage of fixation of specific gravity has been reached in a case of chronic nephritis, the level of the non-protein nitrogen is a fairly good indication of the amount of renal damage although, in a few cases with severe damage, reliance on one or two determinations which show values near to normal may be quite misleading. In cases with fixed specific gravity which show a low non-protein nitrogen, repeated determinations will usually reveal an increasing non-protein nitrogen level. It is in these cases that the determination of the urea clearance is of most value.

A high non-protein nitrogen does not necessarily mean that there is permanent kidney damage and in some instances may not be due to any impairment of renal function.

In acute nephritis, the blood non-protein nitrogen may be very high but, as the condition improves and the blood flow through the glomerular capillaries increases, it subsides.

In the tubular necrosis of metallic poisoning and in lower nephron nephrosis, the non-protein nitrogen increases in direct proportion to the degree of oliguria and, where complete anuria occurs, it may reach very high values indeed. If the patient recovers, the non-protein nitrogen returns to normal and the kidney usually shows no evidence of residual damage.

In acute obstruction to the outflow of urine and in reflex anuria, there is little, if any, actual renal damage but the non-protein nitrogen rises only to return to normal when the urine flow is re-established.

High blood non-protein nitrogen levels may also be found in any condition in which the rate of protein catabolism is markedly increased (for example, high fevers) or in which the renal circulation rate is markedly diminished (for example, severe dehydration or congestive heart failure) without any significant renal lesion being present.

CLEARANCE TESTS

The clearance of any substance is defined as that volume of blood which, in the given case, contains the amount of that substance which is excreted by the kidney in one minute. To put it in another way: it is the amount of blood which, at that particular rate of excretion, could be completely cleared of the substance by the kidney in one minute. This can probably be best illustrated by an actual example. If the kidney is excreting urea nitrogen at the rate of 12 mgms. per minute and the blood urea nitrogen concentration is 15 mgms. per 100 cc. or 0.15 mgm. per cc., the amount of blood which would contain the 12 mgms. of urea nitrogen excreted each minute would be $12 \div 0.15 = 80$ cc.; that is, the urea clearance would be 80 cc. per minute.

In the normal kidney, the method of clearance studies may be used to measure the rate of glomerular filtration if the substance used is excreted exclusively by glomerular filtration and is not reabsorbed in the tubule. There are a number of such substances—inulin, mannitol, and sodium thiocyanate, to mention three which have been used extensively. The amount of inulin, for instance, excreted in the urine in one minute will represent the total amount which was filtered through the glomeruli in that time and, because the glomerular filtrate is essentially a plasma unchanged except for the loss of proteins, the volume of plasma which contains the amount of inulin excreted in the urine will be the

same as the volume filtered through the glomeruli in that time, that is, the plasma clearance of inulin will represent the glomerular filtrate.

In the same way, a substance such as *p*-amino-hippuric acid which is removed completely from the blood by tubular excretion can be used to measure the renal blood flow because its clearance represents the amount of blood flowing through the kidney in one minute. Such a substance will also give a measure of the rate of tubular activity if the level in the blood is raised until it reaches the limits of the tubules' excretory capacity. These measurements are, however, only valid for the normal kidney because any type of tubular damage which would allow the back diffusion of such substances once they were excreted into the tubule would lead to considerable errors in the calculation of the rate of glomerular filtration, renal blood flow or tubular excretory activity. For this reason, the determination of the urea clearance, which is normally the resultant of the rate of glomerular filtration less the rate of back diffusion through the tubules, will give us just as much information about the state of the kidney in renal disease. In addition, it has the advantage that it may be performed without the injection of a foreign substance. The directions for carrying out this test are given in the *Instructions For The Laboratory Course in Pathological Chemistry*.

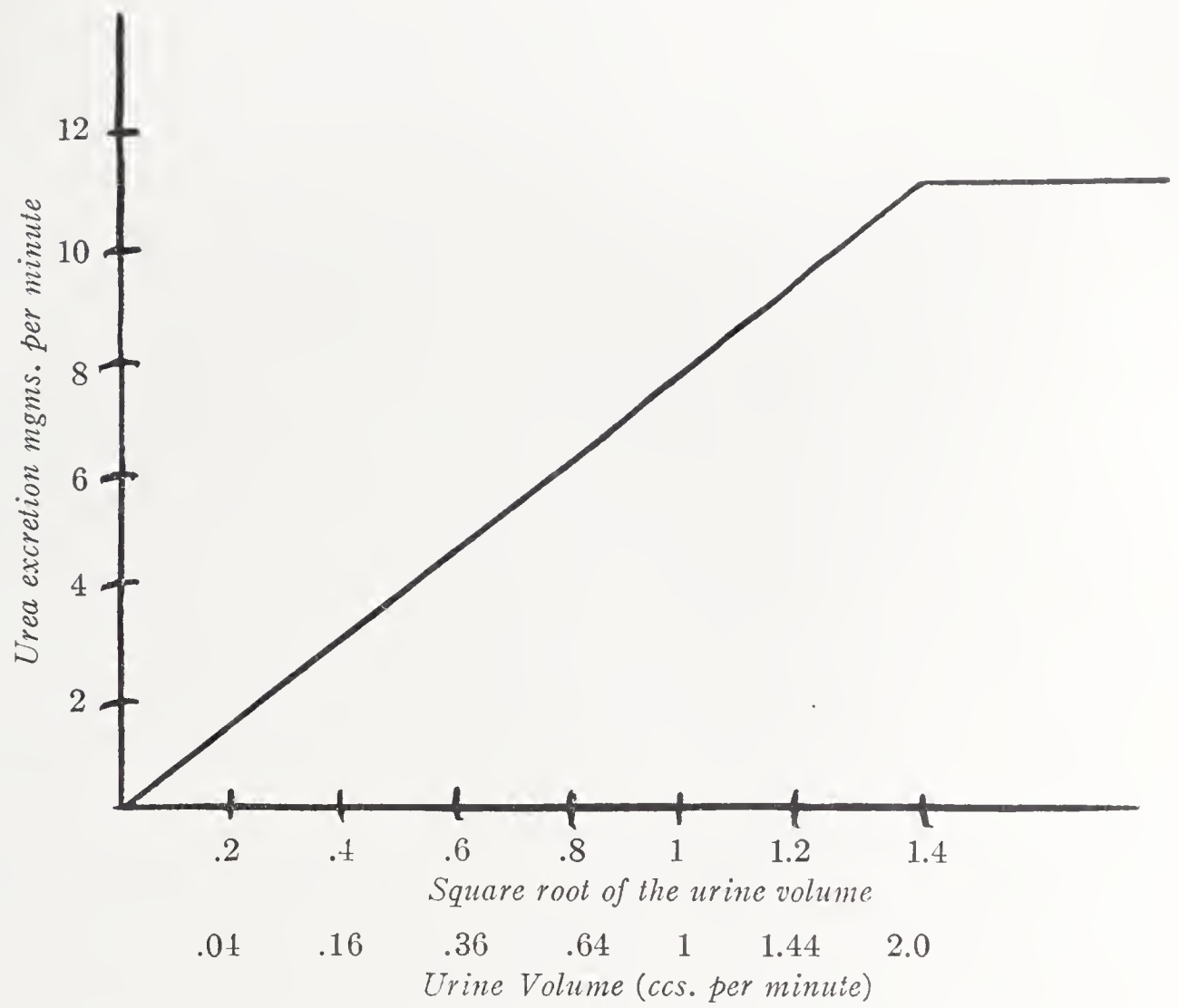
The rate of urea excretion in the normal individual depends on two factors: (*a*) the concentration of the urea in the blood and (*b*) the rate of urine flow.

The first factor determines the amount of urea which will be filtered through the glomeruli and the second, the amount which diffuses back through the tubules. It must be remembered that urea is a substance which is ordinarily freely diffusable through all cell membranes and that the cells lining the convoluted tubules have to perform work to prevent the urea from diffusing back into the blood with the water which is being reabsorbed. They are not able to perform this task completely and even at high rates of urine flow, about 35% of the filtered urea goes back through the walls of the tubules into the blood. As the rate of urine flow becomes less and the concentration of the urea in the tubular urine greater, an increasing proportion of the urea diffuses back. Studies of urea excretion with varying rates of urine flow and a constant level of blood urea during each series of observations show that the rate of excretion is proportional to the square root of the urine volume until the urine flow reaches a level varying from 1.7 to 2.5 cc. per minute in different individuals. Once this rate of urine flow has been reached, the rate of urea excretion becomes independent of the urinary volume. Further increases in urine flow do not result in greater urea excretion but simply in a decrease in the concentration of the urinary urea. This point of change in rate of urea excretion is referred to as the augmentation limit and, for purposes of calculation of the urea clearance, is taken to be 2 cc. per minute, the average of the observed values.

This relationship between urine flow and urea excretion and the effect of the augmentation limit at a blood urea nitrogen level of 15 mgms. per 100 cc. is illustrated in Figure 2.

If two points on the sloping part of the curve below the augmentation limit are taken, they will serve to show in

FIGURE 2



The relation between urine flow and the rate of urea excretion.

actual figures the relationship between urine flow and urea excretion.

At a urine flow of 0.36 cc. per minute, the amount of urea excreted per minute is 4.7 mgms. and, at a urine flow of 1.7 cc. per minute, it is 10.2 mgms. The square root of 0.36 is 0.6 and the square root of 1.7 is 1.3. It is easily seen that the minute-rate of urea excretion is roughly proportional to the square root of the urine volume: $10.2/4.7 \approx 1.3/0.6$

CALCULATION OF THE UREA CLEARANCE

The actual urea clearances may be calculated by dividing the amount of urea excreted in one minute by the amount of urea in 1 cc. of blood or more easily by using the formula $U \times V/B$ in which:

U = the concentration of urinary urea in mgms. per 100 cc.,
V = the volume of urine excreted per minute, and
B = the concentration of blood urea in mgms. per 100 cc.

In any one normal individual, for all levels of urine excretion above the augmentation limit the urea clearance is constant. A urea clearance obtained in this range of urine flow is referred to as a maximum clearance or C_m and represents the actual urea clearance. The average normal maximum clearance in an adult is 75 cc. of blood per minute, with a normal variation of 25% on either side of the mean.

At urine flows below the augmentation limit there will be a different normal clearance for each different rate of urinary excretion. This makes it neces-

sary, if the test is to be of any practical value, to have some one standard level of urea clearance as a point of reference to which all the others may be compared and to use an equation for calculation such that the clearances at every level of urine flow will be reduced to that of the standard. Because the rate of urea excretion varies as the square root of the volume of urine and the square root of one is one, the calculation of the clearance on the basis of the square root of the urine volume instead of the actual volume will result in all clearances below the augmentation limit being calculated as though the rate of urea excretion were that which obtains at urine flows of 1 cc. per minute. The equation for the calculation will then be $\sqrt{V} \times U/B = C_s$ where C_s is the symbol for standard clearance, indicating that it is not the actual clearance but the clearance calculated to the standard rate of urea excretion, namely that which is found at urine flows of 1 cc. per minute.

Three calculations of clearances at different rates of urine flow and with a constant blood urea of 15 mgms. per 100 cc. might clarify this point:

(*a*) At a urine flow (V) of 0.36 cc. per minute, a urinary urea (U) of 1350 mgms. per 100 cc. and a blood urea (B) of 15 mgms. per 100 cc.:
The actual clearance,

$$C = \frac{U \times V}{B} = \frac{1350 \times 0.36}{15}$$

$$= 32.4 \text{ cc. per minute,}$$

The standard clearance,

$$C_s = \frac{U \times \sqrt{V}}{B} = \frac{1350 \times 0.6}{15}$$

$$= 54 \text{ cc. per minute.}$$

(*b*) When $U = 810$, $V = 1$ and $B = 15$ the actual clearance is $(810 \times 1)/15 = 54$ cc. per minute and the standard clearance will obviously be the same.

(*c*) When $U = 623$, $V = 1.7$ and $B = 15$ the actual clearance $= (623 \times 1.7)/15 = 70$ cc. per minute, and the standard clearance $= (623 \times 1.3)/15 = 54$ cc. per minute.

It can be seen from these examples that no matter what the urine flow below the augmentation limit may be, the clearance can, by the use of this equation, be compared with the clearance at the standard urine flow of 1 cc. per minute.

The average normal standard clearance has been found to be 54 cc. per minute with a normal variation of 25% on either side of the mean. The urea clearances are usually recorded as a percentage of the average normal, standard or maximum as the case may be, so that one can tell without further calculations if the result falls within the limits of normal. Any clearance which lies between 75% and 125% of the average normal value is considered a normal urea clearance.

In the case of children or very small adults, the value found for V (the volume of urine excreted per minute) should be corrected for the surface area of the individual by multiplying V by the factor $1.73/SA$ where SA is the surface area of the patient in square metres. The surface area may be calculated from the patient's height and weight with the aid of the standard tables used in determining the basal metabolic rate. This correction for surface area is unnecessary in most adults because the normal variation in the urea clearance in individuals with similar surface areas is as great as the variation in surface area in the greater part of the adult population.

The sensitivity of the urea clearance test has been discussed previously in the section on the concentration test.

The chief value of the test is in cases of chronic glomerulonephritis. It is not so sensitive as the concentration test but, from the time that the amount of glomerular filtering surface has been reduced to about three-quarters of the normal until the patient becomes uremic, it gives a reasonably accurate measure of the degree of renal damage. It suffers from the disadvantage that its accuracy depends not only on the reliability of the analyses of the blood and urinary urea but also on the careful timing of the period of urine collection and the obtaining of *all* the urine passed during that period. The test is dependable only where it can be done under careful supervision by competent individuals.

UREA EXCRETION

A consideration of the ways in which the normal kidney handles the varying amounts of urea which are produced by the catabolism of different quantities of protein may be helpful in gaining an understanding of the way in which severely damaged kidneys may maintain the blood urea, and consequently the N.P.N., within normal limits by excreting a large volume of dilute urine. It will be necessary for purposes of illustration to assume a constant urine flow throughout the twenty-four hours, a situation which does not exist normally. However, this assumption will not invalidate the calculations as they will conform to average twenty-four hour urea excretions under varying conditions. At a urine flow of 0.49 cc. per minute (605 cc. per day) and a blood urea nitrogen of 15 mgms. per 100 cc., the concentration of urea in the urine may be calculated from the formula for the standard urea clearance as follows: $(U\sqrt{0.49})/15 = 54$ or $U = 15 \times 54/0.7 = 1155$ mgm./100 cc. Thus there will be a urea-N. excretion of 5.67 mgm. per minute or 8.2 gms. of urea-N. in 24 hours. This is the amount of urea which would be excreted on a protein intake of about 55 to 60 gms. per day. Assume that the protein intake is raised so that the urea-N. to be excreted is 9.4 gms. per day or 6.5 mgms. per minute. If the blood urea-N. remains constant, there must be an increase in the rate of urine flow to excrete the additional urea. Because the rate of urea excretion varies as the square root of the volume of urine, the new rate of urine flow may be calculated as follows:

$$\frac{\sqrt{x}}{\sqrt{0.49}} = \frac{6.5}{5.67} \text{ whence } \sqrt{x} = \frac{6.5 \times 0.7}{5.67}$$

or $\sqrt{x} = 0.8$. The new rate of urine flow, therefore, will be $(0.8)^2 = 0.64$ cc. per minute or 921 cc. per day. Now, if the rate of urea excretion had to be raised to 14.7 grams of urea-N. per day or 10.2 mgms. per minute, the rate of urine flow would have to be raised to $\left(\frac{10.2 \times 0.7}{5.67}\right)^2 = 1.7$ cc. per minute or 2,448 cc. per day.

Another way in which the increased amount of urea can be excreted is by a rise in the level of the blood urea which will result in a greater urea excretion at the same rate of urine flow. At a urine flow of 0.64 cc. per minute and a blood urea-N. level of 15 mgms. per 100 cc. of blood, it has been shown that the rate of urea excretion is 6.5 gms. per minute. If the blood urea-N. is raised to 20 mgms. per 100 cc., the rate of excretion will be $6.5 \times 20/15 = 8.7$ mgms. per minute or 12.5 gms. per day.

What actually happens is a combined increase in urine flow and blood urea. Consider the example in which the rate of urea-N. excretion had to be raised

to 14.7 gms. per day (10.2 mgms. per minute). If all the urea formed from the protein in the diet was to be excreted, it can be seen that if the rate of urine excretion is raised to 1 cc. per minute the rate of urea excretion will rise to $5.67 \times \sqrt{1}/\sqrt{0.49} = 8.1$ mgms. per minute. At this rate of urine flow, it is obvious that if 10.2 mgms. of urea-N. are to be excreted per minute, the blood urea-N. must rise to $15 \times 10.2/8.1 = 19$ mgms. of urea-N. per 100 cc. of blood, a level well within the normal limits. These illustrations show the way in which the normal kidneys can maintain the level of the blood urea nitrogen within normal limits. Somewhat similar mechanisms are called into play when the kidneys' efficiency is impaired in chronic nephritis.

If the efficiency of the kidney is reduced to 60% of normal, the urea output at urine flows of 1 cc. per minute and a blood urea-N. of 15 mgms. per 100 cc. would be reduced from the normal of 8.1 mgms. per minute to 4.86 mgms. per minute. In order to continue to excrete the same amount of urea, the rate of urine flow would have to be increased and the blood urea level raised. In the normal kidney, at a urine flow of 2 cc. per minute, the rate of urea-N. excretion would be 75 (the amount of blood cleared of urea at above the augmentation limit) $\times$ 0.15 (the level of the blood urea-N.) = 11.25 mgms. per minute. With the clearance reduced to 60% of normal, the amount of urea-N. excreted would be 6.75 mgms. per minute, tsill below the level of 8.1 mgms. per minute which has to be excreted. The blood urea-N. would therefore rise to $15 \times 8.1/6.75 = 18$ mgms. of urea-N. per 100 cc. of blood. This excretion of nitrogen is the amount necessary on a protein intake of about 80 grams per day. If the protein intake is reduced to about 65 grams per day, which is quite a common level of protein intake a urinary excretion of 6.75 mgms. of urea-N. per minute would be required. This could be attained simply by raising the blood urea-N. level from 15 to $15 \times 8.1/6.75 = 18$ mgms. per 100 cc. without any increase in urine volume.

If the urea clearance has been reduced to 40% of normal, the excretion of urea-nitrogen at urine flows above the augmentation limit and a blood urea of 15 mgms. per 100 cc. will be $75 \times 0.15 \times 40/100 = 4.5$ mgms. per minute. To excrete 8.1 mgms. per minute the blood urea-N. level would have to be $15 \times 8.1/4.5 = 27$ mgms. per 100 cc., slightly above the upper limit of normal. If, however, the protein intake is somewhat lower so that only 6.5 mgms. of urea-N. per minute need to be excreted, this can be done at a blood urea-N. level of $15 \times 6.5/4.5 = 22$ mgms. per 100 cc. which is within the normal limits.

These illustrations demonstrate the manner in which the blood urea-N. levels are maintained within normal limits in spite of a considerable degree of renal damage and a protein intake which does not differ markedly from the average.

REFERENCES

(1) A. S. Alving and D. D. Van Slyke: J. Clin. Invest. **13**, 969 (1934)

(2) J. M. Hayman, J. W. Martin and M. Miller: Arch. Int. Med. **64**, 69 (1939)

(3) D. A. Rytand: Arch. Int. Med. **59**, 837, 848 (1937)

TREATMENT OF OCULAR INJURIES IN GENERAL PRACTICE[1]

A. J. ELLIOT, M.D.[2]

ALTHOUGH MANY serious injuries of the eye require hospitalization and the surgical care of an ophthalmic specialist, there are a large number of ocular injuries which the general practitioner may well care for and to which he can render the appropriate treatment.

FOREIGN BODIES

Small sharp objects often become firmly fixed upon the conjunctiva or cornea. Very frequently, the small foreign body becomes lodged underneath the upper lid and may be retained for a long time, producing much irritation and some discharge. It may be overlooked unless the lid is everted. The upper lid may be everted by placing a small probe or a thin pencil horizontally along the skin at the level of the upper border of the tarsus. With the patient looking down towards his feet, the lid is everted by seizing the lashes and drawing the lid away from the globe. The foreign body is usually easily located and removed with a small spud or cotton tooth pick. If there is considerable irritation present, warm, wet compresses three times daily are advised, followed by the instillation of a soothing antiseptic eye ointment, such as boracic acid, 10%, into the fornix.

Particles of steel and emery frequently become imbedded in the cornea, penetrating into the epithelium or corneal stroma. A record of the visual acuity in both eyes should be obtained before the foreign body is removed and at the termination of the treatment. The cornea should be anesthetized with a suitable local anesthetic, for example, Pontocaine (1%) drops or Butyn (2%) drops, and the cornea thoroughly examined under strong artificial illumination. It is sometimes not easy to discover a foreign body upon the cornea. A small lens is very useful in focussing the beam of light on to the cornea. Having located the foreign body, it should be removed with a sterilized spud. Frequently, a brownish rust-ring remains at the site of the imbedded foreign body and it is often difficult to remove this in its entirety at the first visit; in these cases it is better to remove the rust-ring the following day when it has become loosened and in some cases removal of the rust-ring should be carried out piece-meal over a 2 or 3 day period. If the cornea or conjunctiva does not appear to be infected, an antiseptic ophthalmic ointment (e.g., metaphen or boracic acid) should be instilled into the lower fornix and a snug-fitting patch applied to the eye. The patient should always be examined the following day and the cornea stained with aqueous fluorescein, 1%, to determine whether the epithelium has completely regenerated. Atropine should not be used routinely, as it is generally unnecessary, and also produces prolonged blurring of vision, sometimes for days after the cornea has completely healed. However,

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if the eye is irritable and remains painful, atropine may well be instilled with resulting amelioration of pain and marked improvement in the patient's symptoms. The eye should be patched continually until the cornea is completely healed. Cocaine drops are not recommended as a local anesthetic because the corneal epithelium rapidly becomes desquamated with its use. The continued use of cocaine as a local anesthetic without a dressing predisposes the eye to infection—the one complication which is feared in corneal foreign bodies.

The immediate removal of multiple foreign bodies in the cornea is sometimes unwise, as the manipulation necessary for their removal may do more harm than good. A protective dressing and removal of the more prominent ones at the first visit is often sufficient, the remainder being removed at subsequent visits or falling out of their own accord.

The frequency of imbedded foreign bodies in the cornea and the loss to industry involved in these cases, emphasizes the necessity of the physician advising the use of protective goggles and other safety measures. Industrial workers should be educated to go directly to the First Aid station for proper care, and warned against allowing their fellow workers to attempt the removal of the foreign body.

Large particles of steel and, less commonly, stone or glass, may perforate the globe. The foreign body may be so small and the accident happen so quickly that the patient may not experience much pain. There is immediate loss of vision and if infection occurs, successful removal of the foreign body is not easily effected. These cases should be referred for specialized ophthalmic care.

Intraocular foreign bodies may be overlooked for several days. When a history of hitting metal on metal is given, such as hammering, a careful examination of the eyes with x-ray studies of the orbit should be made and if there is a suspicion of an intraocular foreign body the case should be referred for further care to an eye physician.

BURNS AND CHEMICAL INJURIES

Burns by hot water, steam, hot ashes, molten metal, caustics (such as lime), strong acids or alkalis endanger the eyes in two ways, namely, by injuring the cornea and by producing adhesions between the lids and the eyeball. The immediate care of severe burns is that of protecting the globe by frequent instillation of non-irritating oils and ointments. If the burn is caused by caustic, the excess of the material must be removed by copious irrigation with water. If the burn is severe, the patient must be admitted to hospital and treatment instituted to prevent adhesions between the eyeball and lids by using a glass rod well coated with boracic acid ointment. Usually the cornea is involved and in these cases, atropine ointment should be instilled daily. In the most severe cases, daily treatment with vaseline or boracic acid ointment will usually allow the tissues to heal satisfactorily. An eye patch should be worn until the denuded surface of the conjunctiva and cornea are well healed. The prognosis should be guarded, however, and care taken to impress the patient with the gravity of the injury and the necessity for continued supervision.

Exposure to infra-red and ultra-violet light rays frequently results in an acutely red eye. In such cases the

history is important, as the patient must be within a distance of 8 feet from the offending source of light and must be exposed for approximately 30 seconds. The eye condition should be manifested within from 8 to 12 hours. An anesthetic ointment, such as epinephrine, 1:4,000, and butyn, 2%, followed by a patch on the eye usually relieves the congestion in from 24 to 36 hours.

OCULAR CONTUSIONS

Injuries by blunt instruments vary in severity from a simple corneal abrasion to rupture of the globe. The cornea may suffer a simple abrasion from a scratch by a child's finger. The abrasion may be recognized by the green stain on the cornea following the instillation of aqueous fluorescein, 1%. There is usually considerable pain, tearing and sensitivity of the eye to light. In these cases, boracic acid ointment and a snug-fitting eye patch, changed daily, usually will suffice and the cornea heals in a few days.

If the contusion is more severe, there may be a small hemorrhage in the anterior chamber lying in front of the iris. The pupil is often large and reacts sluggishly to light stimulation. The iris may be torn away from its ciliary attachment for a variable distance. Treatment consists of rest in bed and the application of cold compresses several times a day until the hemorrhage is absorbed. Atropine should never be used as an acute glaucoma may result because of blockage of the filtration angle in the anterior chamber by red blood cells. All cases in which a hemorrhage occurs within the eye should be given a guarded prognosis, and in some cases it is wise to admit the patient to hospital.

Case Report:

J.C., a male, aged 12, was hit in the right eye by a small rubber ball following which there was a loss of vision. On examination, 12 hours later, there was a frank, small hemorrhage in the anterior chamber; the vision was 20/20-2 and the pupil reacted sluggishly to light. The tension was normal. He was admitted to hospital, kept quietly in bed, and the hemorrhage in the eye rapidly cleared up. Two days later, in the middle of the night, he suffered a severe pain in the eye with marked loss of vision. On ophthalmoscopic examination the fundus details were not visible; the eyeball was soft to the palpating finger and there was marked circumcorneal injection. The patient was kept in bed for another week at which time the secondary hemorrhage from the iris absorbed completely and the vision returned to normal.

Treatment of the more serious complications of contusions of the eyeball such as dislocation of the lens, detachment of the retina, hemorrhage into the vitreous, and rupture of the choroid, require the care of an ophthalmic specialist.

Fractures of the walls of the orbit frequently produce emphysema in the tissues of the orbital lids. This is due to a communication with the nasal air sinuses, air being forced into the orbital tissues with the blowing of the nose. There is great swelling with a peculiar, soft crepitation on palpation of the eyeballs. X-ray examination will usually demonstrate a small fracture. The treatment of simple contusions with ecchymosis of the lids requires only cold compresses. Emphysema should be treated with a pressure bandage and all straining, blowing of the nose, etc., should be avoided.

LACERATIONS OF THE LIDS

Lid lacerations should be repaired at once, unless signs of infection are already present, the edges being apposed as accurately as possible with fine silk.

These lacerations may be either horizontal or vertical. The horizontal ones take the general direction of the fibres of the Orbicularis muscle and do not tend to gape. They usually heal without appreciable scar formation and require few sutures. Vertical wounds tend to gape widely and a serious deformity of the lid results if careful apposition is not secured. Lacerations through the lid margin require meticulous repair if the result is to be both cosmetic and functional. The least debridement possible should be done, and fine silk sutures on atraumatic needles used. The most important suture to be placed is that uniting the intermarginal groove. This is the grey line situated between the openings of the Meibomian glands and the eyelashes. The lid border will be in perfect alignment if the first suture placed passes through this line, down into the substance of the tarsus, and then across the line of laceration to enter the tarsus at the same distance from the lid border and comes out in the intermarginal line on the other side of the laceration. The sutures and knots should never be left in contact with the corneal surface because the movement of the globe will cause abrasion and scarring. In the care of severe lacerations where dirt has been carried into the wound, it is safest to give a prophylactic injection of antitetanus serum.

LACERATIONS OF THE CONJUNCTIVA

These usually heal spontaneously and require suturing only if there is wide separation of the edges of the wound. Sub-conjunctival hemorrahge should be treated with cold compresses for the first 48 hours, after which time absorption of the blood may be hastened by the use of heat.

CONCLUSION

I have reviewed the treatment of ocular injuries which may be well cared for by the general practitioner. The majority of such injuries can, and should be, the responsibility of the physician first seeing the patient. In all cases, it is important to record the visual acuity at the outset and at the termination of treatment because, so frequently, this information is required if further care is necessary, or if, subsequently, compensation for loss of vision is sought. The physician would be well advised to refer the more serious ocular injuries immediately to an ophthalmic specialist for more detailed examination and treatment.

SUMMER INTERNSHIP IN A HEALTH UNIT

A. RAPOPORT, 4T9

LAST SUMMER saw the unveiling of a new opportunity in the sphere of summer internships for medical students. For the first time in Ontario, and perhaps in Canada, a student was invited to observe and, more important, to partake in the activities of a suburban health unit. The idea and its realization derive from the joint efforts of Professor M. Brown of the School of Hygiene of the University of Toronto and the East York-Leaside Health Unit under the direction of Dr. W. Mosley, Medical Officer of Health and Dr. J. Parker, Assistant Medical Officer of Health, who, sponsored by their Board of Health, provided the facilities, including a fellowship, for this innovation.

The object in making available this internship was to enable a medical student, while yet an undergraduate, to examine in detail one instrument striving to maintain the health of a community at a satisfactory level. The internship is not regarded as a recruitment plan seeking to swell the ranks of the public health workers. While it is hoped that some of the students who undertake this work will be attracted thereby to a career in Public Health, nevertheless there is absolutely no obligation on their part to pursue this branch of medicine. Rather, it is the hope of those in charge that from this "field work", complementing as it does the didactic training acquired at medical school, will evolve an attitude of mind which will cling to the future physician and colour his endeavours regardless of the sphere of medicine in which he may choose to practise. This attitude may be depicted as a sort of medical Weltanschauung in which Prevention is a philosophy of action embracing the welfare not only of individuals but of communities, nations and indeed the world; a philosophy in which health is viewed not merely as the negation of illness but as a positive attainment in itself. More specifically the student will learn the many ways in which the local health department can be of help to the physician and, in return, the manner in which the physician can co-operate to raise the prevailing health standards.

The success of the past summer has prompted those in charge to plan the extension of the internship program to include not one, as formerly, but six medical students in Ontario. As the recipient of the first internship offered under this scheme, it is my intention in the remainder of this article to review briefly some aspects of the summer's experiences in the hope that they may shed some light on the practices of a Health Unit and that they may acquaint those third year medical students seeking summer employment with the workings of this new type of internship. While the statistics to be quoted are those of the East York-Leaside Health Unit, the demonstration Unit for the School of Hygiene, nevertheless it should be understood that, qualitatively, the makeup and program as depicted here are representative, in the main, of the twenty-odd health units dispersed throughout Ontario.

It might not be amiss to explain the term "health unit." A health unit represents a banding together of towns,

townships and/or counties, as the case may be, to raise a large enough aggregate of population and, hence, of finances to ensure themselves an efficient, well-equipped and full-time health service. Thus a town, Leaside, and a township, East York, have united in the East York-Leaside Health Unit. Such a union, it is readily appreciated, is an ideal device for providing rural areas with a service heretofore available only in large and wealthy urban centres.

It was the director's feeling that the intern would be more integrated with the Unit if instead of merely observing from the fringe he were to immerse himself in the stream of its activities. Accordingly two projects were devised for me. The first was to survey the active tuberculosis cases of the Unit by examining all its pertinent records to ascertain the proportion of tuberculosis patients who were found by strict epidemiological measures, such as tracing contacts, and those learned of by more "shot-gun" methods such as mass surveys, and by symptom complaints, etc. The results are perhaps sufficiently interesting to note here. Of 328 active tuberculosis cases, only 28 had previously been listed as contacts. Three hundred, therefore, had been found by other methods. This illustrates the limitations of a purely epidemiological approach to the problem of tuberculosis detection and stresses the need for mass surveys. Furthermore only 66 of the patients could list a possible source and many of these were so remote as to preclude all chance of infection spreading from them. This fact points to the need for a more exact definition of how intimate a relationship constitutes a source or a contact, and emphasizes again the great gaps in our knowledge of the epidemiology of tuberculosis.

Needless to say, it was inevitable that, from this study, one would become familiarized with all the intermediate stages in tuberculosis statistics from the private physician to the Onterio Government and the manifold correspondence involved in the tracing of contacts and the admission of patients to sanatoria. Incidentally, visits made to the homes of tuberculosis patients in sanatoria very forcefully displayed the necessity of appreciating the familial and social environments of a patient when prescribing treatment. One can imagine the distress of an invalid in a sanatorium were he overburdened with problems of raising money to pay for his treatment and upkeep there and the maintenance of his family at home. Fortunately the humane measures taken by the Ontario Government have obviated both these considerations. This broader view of therapy can perhaps better be evaluated in a unit where homes are visited and family tensions witnessed than in a hospital where the patient is a "case" occupying a bed and seemingly divorced from his surroundings.

The second project was to survey by home calls some of those houses in East York which had not installed plumbing and sewage facilities. Among the data collected were the conditions of the houses, the numbers of rooms and the conditions of what disposal means were available. It will come as no surprise to learn that this state was most prevalent in the poorer section of the Township. This study was invaluable for demonstrating the social and economic forces which influence the health program of an area and which must be contended with if such a program is to be successful.

Very revealing were the tours made with the two sanitary inspectors of the

Unit. These included routine inspection of swimming pools, restaurants and food and packing plants. Many were the trips made to investigate "nuisance" complaints. These ranged from the keeping of pets by neighbours to the tenant's children soiling the dwelling. One could not help but be astonished, in certain cases, at the solicitude shown for community health by some plaintiffs when it was obvious that their own properties were anything but paragons of cleanliness.

Equally significant and more provocative of human interest were the visits made with the Public Health Nurses, twelve of whom comprised the staff of the Unit. All mothers in the area are visited about a month post partum and are given advice regarding the care of their infants. They are encouraged, as well, to attend the Child Health Centres and Immunization Clinics sponsored by the Unit. The tuberculosis program constitutes a large part of the nurses' activities and the very soul-stirring drama of household disruptions due to this disease has already been suggested. Random visits such as inspecting a house to determine its suitability as a boarding home for children or calling on a lonely, Old Age Pensioner with no family, to assure her that someone still is concerned with her well-being likewise provided insight into the rays of sociology waiting to illumine medicine in order that the latter may more fully exploit its potentialities.

A more or less scheduled event was the weekly afternoon visit at the Child Health Centre known more colloquially as the "Well Baby Clinic." Here, a physician with the assistance of nurses and volunteer workers gives physical examinations to babies brought in for the first time, adjusts formulae as required and notes the progress in weight and appearance of these infants. When treatment is required, the mother is referred to her family physician. This is quite in keeping with the policy of the Health Unit—that of not competing in any manner with the local physicians but rather of assisting them and complementing their services. Physicians in practice are not only encouraged to cooperate with the Unit but in certain instances are actually engaged to perform its functions.

Easily among the most fruitful proceedings of the summer were the discussions held at the office by the Staff, visiting Health Officers and Welfare Officials. At these, the pros and cons of a great host of issues, medical and otherwise, were considered. It is readily understood that by partaking in such sessions one garners a world of information and, furthermore, finds one's channels of thought deepened and made to flow in new fields.

In conclusion, may I point out that the foregoing account is in no way an exhaustive description of the protean activities of a health unit. Rather, it is my hope, that the goals and offerings of a new type of internship have been adequately depicted for those students who may be interested and that, perhaps incidentally, some information may have been imparted concerning the workings of but one link in the administrative chain of our Health Department.

In closing, may I thank Doctors Brown, Mosley and Parker for conferring upon me the opportunity that is this internship and for rendering my sojourn at the East York-Leaside Health Unit so profitable and so pleasant.

THE PLACE OF PHYSICS IN MEDICAL TRAINING

R. W. McKAY, M.A., PH.D.*

THE pre-medical student is anxious to undertake at once the study of those subjects which are obviously related to the practice of his chosen profession. Apparently irrelevant training arouses his impatience because it postpones the time when he can alleviate the ills of suffering humanity or attract paying patients to his shingle. When he wonders why he should study physics, for example, he may be given one of three answers. First, the regulations require it. Second, physical knowledge finds numerous applications among the tools of his trade. Third, physics is the simplest science and its study provides a reasonable training to anyone who wishes to grasp the greater complexities of medical science.

The eminently practical basis of the first answer cannot be refuted. Both the regulations of his school and the laws of the province require him to possess some familiarity with the elements of the fundamental sciences. Such regulations have the support of custom and authority. While this insistance on the study of physics does not go back continuously to Galen or Hippocrates, though they, themselves, were well versed in the science of their day, it does date back nearly to the earliest state-approved curricula for medical training. In England, for example, the Council on Medical Education's first list of subjects, "without a knowledge of which," medical registration was not permitted, did not include physics. This omission was rectified within fifteen years, however, when physics was added in 1885 as a compulsory subject. It was not until thirty years later that anesthetia and medical ethics were added to the curriculum.

But some students will look further for the reasons underlying even a universally accepted custom. They will find the second answer more convincing. Applications of physics in medicine they will see wherever they look. Examples may be found from any branch of physics. Consider mechanics, which has perhaps the least obvious connection. The principles of forces and levers underlie the action of the skeleton and muscles. Acceleration is important in motion sickness and in aviation medicine. Examples of periodic systems are found in the heart and diaphragm. The concept of energy is basic to the study of metabolism. Measurement of blood pressure is an almost purely mechanical technique. The list could continue indefinitely.

The applications of heat and electicity are numerous, both in the physiology of the human body and in much of the apparatus of diagnosis and therapy. The ear and the eye are organs whose complex functioning cannot possibly be understood unless their behaviour as acoustical and optical instruments is first known, and, of course, those symbols of the doctor's calling, the microscope and the stethoscope, are also applications of optics and acoustics.

It might be of interest to consider the possibilities of some of the more recent applications. As histology and bacteriology are dependant on the microscope,

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some new science, the importance of which one cannot guess, might grow from discoveries waiting to be made with the electron microscope. This instrument allows the observer to see objects of molecular dimensions. The fact that the specimen must be examined in a vacuum may somewhat limit its usefulness, but the extent to which the electron microscope has already been used suggests that this limitation may not be too serious.

Artificial radioactive materials offer a number of very interesting possibilities both in medical research and practice. Radioactive forms of the common elements such as carbon, sodium and iodine can be produced which are chemically identical with the ordinary forms of these elements but which differ in some physical properties. In particular, they give off radiations which allow the presence of extremely small traces to be detected readily by electrical methods. In effect, this allows one to label certain atoms which can then be followed throughout their subsequent reactions without, in any way, affecting the course of the reactions. The availability of strongly radioactive materials also has possibilities of usefulness for therapy with the radioactivity associated with chemical properties which can cause the treatment to localize itself in bones or glands.

The third answer may now be considered. The complexities of some of the applications are such that they could not be grasped by the elementary student, and the techniques change so rapidly that detailed methods studied now might well be obsolete in a few years time, but the underlying principles which are essential to a true understanding of any application are relatively permanent. Moreover, physics is essentially the simplest of the sciences. In physics it is possible to reduce many problems to their simplest form without irrelevant matters. In living material the unit is the cell, but even if the cell could be studied alone, it still remains a complex system of interacting protein molecules, and the structure of the protein molecules themselves is only known in barest outline in spite of an enormous amount of research in this field. In contrast, the motion of a ball hanging on a string, or the falling of an apple from a tree appears childishly simple, yet these were subjects which interested Galileo and Newton and helped in the formulation of basic principles.

The observation of experimental processes and their quantitative relationships, and the reasoning which leads from the particular case to the general law are basic to all scientific research and practice. These scientific methods can best be learned in such simple cases as are provided in elementary physics. One vital exception to this statement might be noted. The very fact that random variations due to uncontrolled factors can be largely eliminated in elementary physical experiments, makes the treatment of these variations appear of secondary importance. In the so-called, less exact sciences however, the prominence of random fluctuations causes the application of statistical methods to assume its true importance. Yet, strangely enough, it is frequently assumed that familiarity with the statistical interpretation of data should result from an elementary course in physics.

A PROBLEM IN DIAGNOSIS

MISS BARBARA McKINNON, 4T9

PRESENTATION OF CASE

Mrs. V. L., a forty-seven year old, white woman, moderately disabled by chronic rheumatoid arthritis, was admitted to the Private Patients' Pavilion, Toronto General Hospital, with a diagnosis of acute appendicitis. Two days before admission, she developed epigastric pain of gradual onset which, after a short time, settled in the right lower quandrant. It was aggravated by turning in bed and by local pressure. The pain was accompanied by vomiting and constipation which later changed to diarrhea. There was no history of any previous episode of a similar nature.

On admission, she appeared acutely ill. Her breath had a fetid odor. Her chest was clear on physical examination. Abdominal examination revealed decreased movement on respiration, moderate rigidity, and rebound tenderness over McBurney's point. There was high, right-sided tenderness on vaginal examination, The pulse rate was 138; the temperature, 103° F.; the white cell count, 17,200; and the blood pressure, 142 mm. systolic and 86 mm. diastolic. Examination of the urine revealed 20 - 25 white cells and occasional red cells per high-power field but no other abnormalities. The diagnosis was acute perforated appendicitis.

Through a right rectus incision, the gangrenous, perforated appendix was removed and from the right iliac fossa, a sero-purulent material was aspirated, which, on culture, grew *E. coli* and streptococci. Penicillin (300,000 units) and streptomycin (2 gms.) were put into the peritoneal cavity. The peritoneum was tightly closed. A Penrose drain was left superficially in the wound. Treatment was then directed toward the generalized peritonitis employing Wangensteen suction, penicillin and streptomycin.

The first complication arose on the day following the operation, with the development of anuria, then oliguria, with varying amounts of albumin, red cells, white cells, hyaline and granular casts, and epithelial cells in the urine. The non-protein nitrogen level rose to 100 mgm. per 100 cc. and there was a moderate degree of acidosis. There was slight edema of the legs. The urinary excretion returned to normal by the tenth post-operative day with only intravenous fluid therapy.

The second complication presented on the third postoperative day in the form of patchy signs of consolidation in the left lower lobe posteriorly without pleural pain, cough or sputum. The pulse and temperature remained elevated.

On the sixth post-operative day, in spite of signs of resolution in the left lung, an area of bronchial breathing developed in the right base, with some pleuritic-type pain anteriorly. There were no complaints of cough or sputum. An x-ray on the twelfth post-operative day showed an opacity in the right base with a small pleural effusion. The temperature continued to swing to 101 or 102° F. daily. The white cell count at this time was 9,100.

In addition to the pulmonary signs and symptoms, some tenderness and

induration in the right lower quadrant of the abdomen developed on the eleventh post operative day. This quickly localized to a tender, mobile, non-fluctuant mass deep to the incision. Associated with this was marked diarrhea. The incision was opened the following day and there were removed eight ounces of foul green pus which, on culture, grew *E. coli* and streptococci. A drainage tube was left in the incision. The temperature approached normal for one day, and then resumed its spiking qualities.

On the fourteenth post operative day, rigidity and splinting were noted in the right upper quadrant. Fluoroscopic examination on the twenty-first post-operative day showed a high right diaphragm with decreased respiratory excursion. The right costo-phrenic angle was obscured. Chest aspiration was carried out on the following day and a pocket of foul pus was found two and one-half inches from the skin surface in the eighth interspace at the right posterior axillary line. It was felt that the needle was in the subphrenic space. The pus was cultured and grew *E. coli* and streptococci. Following the aspiration, the temperature fell transiently.

Surgical exploration of the subphrenic space posteriorly on the twenty-third postoperative day failed to reveal a subdiaphragmatic abscess. The assumption following this was that the pus was above the diaphragm forming a localized empyema. During the next twenty-four days, the chest was repeatedly aspirated and penicillin was put into the cavity. However, the signs in the right lung base did not diminish, nor did the temperature return to normal. After lipiodol was injected into the space, an X-ray (see figure 1) showed two cavities, one above and one below the diaphragm, with a sinus between them. An operation was performed.

Fig. 1: Right lateral chest film showing lipiodol in abscess cavities above and below the right diaphragm, with sinus connecting them. (Film reversed in preparing illustration).

DIFFERENTIAL DIAGNOSIS

Anuria and Hematuria

Because of the presence of tubular casts, which indicate true renal disease, it is unlikely that the anuria could have been due to a *reflex* suppression of urinary excretion due to the inflammatory process within the peritoneum. More

probably, there was an *acute toxic nephrosis* with moderate damage to the epithelium of the distal convoluted tubules. This could have been due to a toxic reaction and to post-operative collapse with decreased filtration pressure and anoxia. The fact that this patient had no sulphonamide therapy before or after the operation rules out the possibility of a *sulphonamide reaction* in the kidney tubules.

Pulmonary Complications

The problem of arriving at a correct diagnosis of the pulmonary sequelæ is a difficult one. In retrospect, each step in the pathological process is obvious, but dealing with the clinical signs as they appeared was not straightforward, as is evidenced by the long duration of the acute illness.

The signs of consolidation in the left lung base could have been due to *infarction*, *pneumonia* or *postoperative atelectasis*. The absence of cough and sputum, and the knowledge that this patient was particularly limited in respiratory exercise by peritonitis and by arthritis, makes the diagnosis of atelectasis the most likely one.

The same differential diagnosis with the same conclusions may be offered for the right lung in its early stages. Signs appeared at the right base on the sixth postoperative day and it is to be remembered that the *thoracic complications* of a *subphrenic abscess* following a perforated appendix would occur on or about the tenth day at the earliest. The possibility that an infected embolus caused a *pulmonary infarct*, then an *empyema*, could have been considered, in spite of its rarity, before the demonstration of an abscess below the diaphragm.

It is known that an *appendiceal abscess* developed on the eleventh day. From this *E. coli* and streptococci were cultured—the same organisms as were grown from the empyema pus. The presence or absence of a *subphrenic abscess* at this time is not known. The diaphragm has a rich plexus of lymphatics draining upwards from the peritoneal cavity to lymph nodes lying between the superior surface of the diaphragm and the pleura. Organisms may reach these nodes from any infection in the peritoneum. Pus loaded with organisms arising from a subphrenic abscess could feed an empyema cavity through a penetration of the diaphragm. Again, such an abscess itself could well cause immobilization of the diaphragm on that side, with collapse of the lung base and the development of a sterile effusion. It is also known that a subphrenic abscess may be handled adequately by the body defenses, while spontaneous recovery of the associated empyema is rare.

In a series of three hundred cases there was only one case of subphrenic abscess arising secondarily from an empyema and it was almost certainly due to operative trauma (Coope: *Diseases of the Chest*).

CLINICAL DIAGNOSIS

Perforated gangrenous appendicitis
Acute toxic nephrosis
Postoperative atelectasis

Subphrenic abscess, developing secondarily to the appendicitis, with an associated sterile pleural effusion which later became an *empyema* encysted above the diaphragm.

TREATMENT AND CLINICAL COURSE

The treatment of this case was complicated by the difficulty in diagnosis. Massive doses of streptomycin and penicillin were used immediately following the operation. Because some strains of *E. coli* are insensitive and others possibly become resistant to the streptomycin, this drug was discontinued after three days. The penicillin was continued in intermittent courses in an effort to combat the streptococci demonstrated. A trial on medical treatment of the empyema by repeated aspiration and antibiotics was carried out because it was felt that the exploratory operation had ruled out any possibility of infection below the diaphragm. However, the empyema was being continually fed from the subphrenic abscess, explaining the failure to control the swinging temperature. This, in fact, remained as the presenting sign which perpetuated the search for a focus of infection, for the patient was, subjectively, in excellent condition. Following the radiological demonstration of the two cavities, with penetration of the diaphragm, both cavities were drained through an anterior abdominal incision on the fifty-second day following her initial operation for appendicitis. She recovered dramatically: the temperature fell to normal, the chest signs cleared and she was discharged eight days later with only a slight serosanguinous discharge coming from the drainage tube.

ACKNOWLEDGEMENT

I should like to thank Dr. Cameron Gray for his helpful interpretation of the handling of this case, and for his constructive criticism of the presentation.

MALNUTRITION IN CANADA

"Was man weiss, sieht man."

A. HOFFER, B.S.A., M.S., PH.D., 4T9

THE MEDICAL PROFESSION has become increasingly cognizant of the fact that nutrition is of importance in the practice of medicine, but the application of sound nutritional principles to medical problems has been painfully slow. There is a tendency today to underestimate the prevalence of faulty diets among the general population although it is readily recognized that diseases of the digestive system may produce deficiency syndromes. Therefore, the physican fails to watch for and to treat disorders of primarily nutritional origin, and adequately to treat by diet malnutritions associated with, or complicating, well recognized non-nutritional clinical entities. Pett (10) has stated that hospital diets do not meet even the minimum needs of patients, let alone provide the hyperalimentation that can contribute to early convalescence and reduce complications and mortality. It can be readily shown that few, if any, of the diets prescribed for chronic diseases such as diabetes or nephritis are adequate with respect to many dietary essentials.

There are several reasons why practising physicians have lagged in the application of the newer knowledge of nutrition. These include the lack of adequate training in medical colleges, the relative novelty of nutritional research and the scatter of nutritional reports through so many scientific journals unknown to them. They do not appreciate the genesis of deficiency syndromes—that nutritional failure develops in stages. According to Joliffe (5) these are (*a*) tissue depletion, (*b*) biochemical lesions, (*c*) functional changes, and (*d*) anatomic lesions. The essential factor in the genesis of nutritional disorders is time. Only when the deficiency state has been marked and prolonged are the classical or gross nutritional syndromes found. Kruse (6) states that:

> "In the past the mild and chronic states have received only sporadic and scant notice. By nature they have not been likely to attract attention. The mild are not conspicuous; indeed they are below the level of unaided perception. Their associated symptoms, though often troublesome, are not so intense as to be unbearable until therapy has brought relief. The grossly perceptible chronic process comes on so gradually and insidiously as not for a long time to be obtrusive. Only in the advanced state is it likely to draw complaint. Though noted often, little significance has been attached to it. Its relation to nutrition has been unrecognized.
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> Since the chronic state of deficiency disease has not been commonly recognized it is worth while to mention some of its characteristics. Its essence is time. For persons this is age. The longer persons live the more chance they have to incur changes and to have them develop to an advanced state. Consequently chronic changes are seen with greater frequency and in the latest stages with increasing age.
>
> In the past these chronic alterations have been called senile changes with the implication that senility causes them. But senility *per se* is not responsible for them. That has never been a satisfactory explanation. Not all elderly persons show the changes. On the other hand they occur in children. Time, not senility is a dimension over which they progress. They are specific avitaminoses in a state of chronicity, due usually to respective dietary deficiencies running over a period of years. Their prevalence and severity vary with the number and degree of deficient diets and therefore with economic level. Most important of all, they are reversible, yielding slowly but completely to appropriate therapy."

Physicians have reported that, in their experience, nutritional disorders are rare although surveys have indicated that, in reality, they are quite extensive. For example, one official of the United States Public Health Service, during the course of a field trip, was met by the local health officer who assured him that he would find no deficiency diseases in that section. The Public Health representative looked at him and questioned the fissures at the corner of his mouth. The health officer gave some excuse but went on to enumerate other symptoms which were typical of riboflavin deficiency. His symptoms were cleared by treatment with riboflavin and, since then, he has discovered many other cases like his own. As a rule, the physician has recognized only the florid or gross nutritional deficiency disorders.

Furthermore, because the time factor in the genesis of nutritional disorders has not been properly evaluated, physicians have been disappointed in the therapeutic use of certain synthetic vitamins for conditions which have been reported to be due to malnutrition. It appears somewhat illogical to expect to reverse chronic pathologic states such as degenerative changes in the nervous system by vitamin therapy even though these changes may be due to chronic deficiencies.

If there are deficiency states in Canada, the physician must be aware of them in order that he may properly treat his patient. It is the object of this paper to present evidence, based on nutritional studies in Canada, the United States and Newfoundland, which indicates that malnutrition is more common than has appeared to be the case. Methods adopted by these countries to meet this problem will be indicated.

MALNUTRITION IN THE UNITED STATES

More extensive nutritional surveys have been reported in the United States than in Canada. If it can be shown that nutritional deficiencies are widespread in the more prosperous sections of the United States and if the dietary habits of these areas are similar to the dietary habits in Canada, then evidence from these surveys can be used to reinforce evidence obtained from smaller scale surveys in Canada.

According to Joliffe, McLester and Sherman (2), evidence for deficiency diseases are obtained from (*a*) food consumption records, (*b*) official death rates and hospital admission figures, and (*c*) medical assessments of nutritional status in samples of the population.

The evidence from food consumption records and dietary surveys will depend upon the yardsticks adopted for an adequate diet. If these criteria are such as will just support life, the apparent incidence of inadequate diets will be low. If the criteria will prevent malnutrition under physiologic conditions, the apparent incidence will be higher. Finally if the criteria will promote optimal health and well being, the incidence of inadequate diets will be highest. In the United States, the Food and Nutrition Board of the National Research Council has adopted and recommended dietary allowances on the basis of expert opinions, research investigations, and the advice of leading nutritionists, physicians and scientists of the country. These have been the criteria used in most American surveys. It has been claimed, however, that these standards are much too high and that, therefore, the apparent high incidence of deficiency states is fictional.

Most authorities, however, have agreed to these standards.

Evidence from official mortality rates is not reliable because deficiency states have not sufficient historical background to entitle them to an honored position amongst causes of death and are difficult to recognize. The terminal disease is listed as the cause of death even though a nutritional deficiency may have paved the way.

Similarly, hospital admission and discharge studies have not been very reliable. Joliffe and his co-workers state that "like persons with the common cold, patients with malnutrition enter the hospital only when sequelae develop. On discharge, neither the common cold nor malnutrition but only the sequelae appear as the discharge diagnosis." In 1938, at Bellevue Hospital, records show the incidence of dental caries to be 0.68% of all the patients admitted whereas it is common knowledge that the incidence is better than 90% in an adult population.

Medical assessment of populations should yield valuable information. It is obvious that, in our present state of knowledge concerning the diagnosis of malnutrition, there is a wide borderline between nutritional inadequacy and diagnosable malnutrition. This might be called the subclinical phase. It must be distinguished from the clinical deficiency states which are unrecognized due to a lack of methodology and training of the investigator. Assuming that all clinical deficiency states will be recognized, it is impossible to study entire populations. However, if a sufficient number of samples are drawn from that population for nutritional investigation and if, in these samples, evidence of malnutrition is found, then it can be concluded that malnutrition is also present in the total population. Thus, studies of infants, preschool and school children, pregnant women, underprivileged groups, young men of military age and the old age group should show signs of malnutrition if there are any in the total population.

Pennsylvania, according to Mott and Roemer (8), is one of the wealthiest states in the Union and, therefore, lends itself well to nutritional investigations. We would least expect fo find malnutrition there. Extensive nutritional studies have been carried out there and are still in progress, and, according to the School Health Act of 1945, all children in the odd number grades (about 2.5 million) must undergo complete physical and dental examinations. These extensive studies have shown that (*a*) serious dietary deficiencies exist in the food selections of pregnant women, (*b*) poor food habits and gross dietary inadequacies are prevalent among preschool and school children and their parents, (*c*) there are high degrees of malnutrition among all groups of the population, (*d*) there are extensive dietary inadequacies in the meals selected by those children and adults who had rampant dental caries or serious dental diseases, and (*e*) there was marked improvement in physical well-being and nutritional status when specific measures were instituted to improve health. More specifically, detailed studies of 10,000 school children have revealed that 85% failed to exhibit reasonably good nutrition in one or more respects. The following deficiencies were found: protein 52%; calories, 48%; calcium, 48%; iron, 48%; vitamin A, 53%; thiamine, 52%; and vitamin C, 38%. In another Pennsylvania study, of 2400 cases, 53% of the preschool group, 20% of the school group and 25% of the adult group were seriously deficient in one or more dietary essentials.

Another fairly large sample consists of the young, adult males inducted into the Army. Of the first million examined, about 133,000 were rejected as unfit for military service because of disabilities directly or indirectly connected with nutrition. Of those accepted as fit, it is well known that, although there was no demonstratable disease, there was a marked gain in weight and improvement in appetite, bearing and efficiency while in the Army. "A-1" and "healthy" are not identical. It is obvious that the conditions requisite for health were not present in the previous civilian life and work of a large proportion of service men.

Recently, in California, where the nutritional status is probably better than in most sections of the United States, large scale experiments were conducted in order to determine whether an improved diet would result in the production of more airplane propellers and tank treads. There were 1,100 employees in the test. Most of them were young and healthy because they had to pass rigid physical examinations before being hired. Their diets were above average. However, a thorough analysis of their diets indicated that 87% were inadequate with respect to one or more nutrients. Nearly all showed evidence of present or past avitaminosis A; about 20%, of thiamine; and 50% had low vitamin C titres in their sera. There were no gross deficiency states, but 60% reported that they had various vague gastro-intestinal symptoms. These workers were given synthetic vitamins. After one year of study, it was concluded that the administration of vitamins definitely improved the performance of the men. This pragmatic test has so impressed managements that many industrial plants in that area are now routinely giving their employees vitamin preparations.

Mott and Roemer (8) have shown that rural areas as well as urban areas have extensive deficiency states. Contrary to popular opinion, rural areas are less well fed than urban areas.

Comparisons have been made between Canadian and American dietary habits. Comparable groups in Canada and the United States spend about 32 and 35% of their total incomes on food. For all groups, the percentage is slightly higher in the United States. In total food consumption there is a remarkable similarity between diets but American diets tend to be slightly higher in bread and cereals, in meat and fish, and in fats and oils; the same in milk products and eggs and in vegetables and fruits. According to chemical composition as to protein, fat and carbohydrate, the intake of both countries is similar. If, therefore, deficiencies are widespread in the United States we should not be surprised to find them also in Canada.

MALNUTRITION IN CANADA

Among the early nutritional studies in Canada were those by the Nutrition Services of the Department of Pensions and National Health in 1939 and 1940. The findings are summarized in Table I. The standard daily requirements accepted were 6,000 units for vitamin A, 1.5 mg. for thiamine, and 60 mg. for vitamin C.

More recent nutritional investigations have supported these findings. Robertson and Galloway (12) concluded that, in lower income Toronto families, the vitamin C intake was under the minimum requirements in 38% of the children and in 82% of the adults. Pett (10) states that nutritional deficiencies in

TABLE I

DIETARY DEFICIENCIES IN CANADIAN DIETARY SURVEYS 1939-1940.

PERCENTAGE OF PERSONS HAVING DIETS MARKEDLY DEFICIENT (BELOW 70% OF THE CANADIAN DIETARY STANDARD) IN THE INDICATED FOOD CONSTITUENTS

Survey area	Calories	Protein	Calcium	Iron	Vitamins A	Vitamins B_1	Vitamins C
Halifax (low income)	4	4	40	10	34	100	57
Quebec (low income)	1	1	46	8	63	60	13
Toronto (low income)	33	37	60	75	43	93	79
Toronto ($1500-2400)	14	13	13	25	9	61	34
Edmonton (low income)	22	26	43	52	20	84	34

Canada are widespread. From 37% of children in some areas to 91% of children in other areas are getting no source of vitamin D. Up to 14% of children in Canada are receiving insufficient calories and the riboflavin deficiency varies from 22% of the total in Saskatchewan to 0.6% in Ontario. In one Nova Scotian Island, Pett and Hanley (11) found that 76% of the diets were borderline. Only 5.5% could be classed as good. No gross deficiency states were discovered, however 6% of the sample had anemia, 4% were underweight, 13% had present or past evidence of rickets, 5% had probable evidence of a lack of riboflavin and 29% were lacking in vitamin C. Red and swollen gums were found in 14%.

In a fairly conclusive recent study, Ebbs, Tisdall and Scott (3) have directed attention to the importance of adequate nutrition during pregnancy in influencing the course of the pregnancy and the subsequent health of the infant. A total of 400 pregnant women were divided into three groups. One group of 120 were allowed to continue on their inadequate diets, another group of 90 were given supplemental food from the fourth month until the baby was six weeks old and the third group were given only nutritional advice because they were already on fairly good diets. The results were striking. During the course of pregnancy, the mothers in the good or supplemented diets enjoyed better health, had fewer complications and were better obstetrical risks than those consuming the poor diets. The incidences of miscarriages, premature births, and still births among those on the poor diets was much greater. The incidence of mastitis was twice as great in the poor diet group. There were fewer illnesses in babies under 6 months of age from the good diet group, and the mortality rate was many times greater in the poor diet group. A significant statement is made to the effect that "In a large proportion, one could tell the diet group of the mother by looking at her baby."

Ebbs (2) concludes that "Gross nutritional deficiencies are seldom encountered in the population today but as our knowledge of nutrition increases more and more evidence is presented that there are minor deficiencies which impair to varying degrees the health and efficiency of our population. Such minor or subclinical deficiencies which in the average individual would take weeks or months to develop could be

exaggerated and hastened by the increased nutritional needs during pregnancy."

NUTRITION IN NEWFOUNDLAND

In 1944, a very thorough medical survey of nutrition in Newfoundland was made (9). The food supply was investigated, the clinical examination of the subjects and complete biochemical studies of body fluids were correlated. Nutritional deficiencies due to lacks of vitamin A, riboflavin and/or ascorbic acid were very frequent. An appreciable number of people showed evidence of thiamine deficiency. Mild acute and chronic niacin deficiencies were frequent. Few had rickets. The average food supply was adequate in calories, protein and fat but very low in vitamin A, riboflavin and ascorbic acid. The amount of niacin was at recommended levels but calcium was extremely low. Chemical findings reinforced these conclusions. The infant mortality and death rate from respiratory tuberculosis were high compared with the rates for other groups of people of the same ancestry. This is partly accounted for by the poor nutritional status of the people of Newfoundland.

WHAT HAS BEEN DONE

In order that the medical practitioner may properly evaluate the nutritional status of his patients, he must be aware, firstly, that there is the problem of malnutrition and, secondly, what measures have been taken to combat it. In general, there are two philosophies with regard to the proper method of combating malnutrition. In one, emphasis is placed entirely on the value of educating and convincing people that they ought to eat better diets. This is a very important method, but requires the cooperation of public health authorities, dietitians, physicians and the general public. It is a long range program and an extremely difficult one. A tremendous outlay of effort and money is required to persuade any appreciable portion of the public to change their food habits. Where nutritional advice clashes with popular food habits it is practically impossible to persuade people to change their habits. They will eat what they have been accustomed to eat and what they like, not what some one else tells them is good for them.

The other philosophy might be termed a more practical one. It concerns itself with two major objectives: (*a*) the immediate one of improving nutrition by economic measures such as school lunches, lunches to industrial workers, encouragement of the consumption of protective foods and, finally, recognition of the fact that because a large proportion of the population is unable to afford the protective foods which they are advised to eat and would eat if their income permitted, some attempt must be made to assist them in obtaining their requirements; and (*b*) the long range one of educating and leading the population toward the pathway of better nutrition.

In the United States, the second philosophy has been adopted. Better nutrition has been encouraged in many sections of the country and, in addition, the enrichment of white flour with synthetic vitamins has been introduced. It has been estimated that bread accounts for approximately one-quarter of the total caloric intake of both American and Canadian diets. It is thus logical to use flour as a carrier to supply essential nutrients to the population. It is also well known that the con-

sumption of bread increases as the income of the family decreases or as the caloric expenditure per worker increases. Because modern white bread is deficient in thiamine, niacin, iron and calcium, it was proposed that white flour be enriched with synthetic vitamins. Many nutritionists have advised that whole wheat bread be consumed instead of white bread. It is not proposed here to enter the argument of white *versus* whole wheat bread because no one will deny that whole wheat bread is nutritionally sounder, in many respects, than white bread. However, it is a fact that Canadian and American consumers insist on eating white bread. It has been very difficult to persuade any appreciable proportion of the public to consume anything but white bread unless the exigencies of total war, as in Great Britain, force them to do so; but, even so, they do not like it. It is possible to increase the consumption of whole wheat bread but, where there has been a free choice, the population has invariably selected white bread. A practical illustration is the experience in Switzerland in 1937-1939. A drive for increased consumption of 85% brown flour (containing 85% of the entire wheat kernel) was started in 1936. In 1937, all millers were ordered to produce only this flour. By means of a thorough educational campaign and a government subsidy, consumption rose to 75% of the total in January. Thereafter, the consumption rapidly dropped to 20% by April, although the government subsidy of 25% was continued. When the subsidy was reduced to 12.5%, consumption dropped to 10% of the total by the middle of 1939, which was the proportion of brown bread consumed before the inauguration of the program.

In the United States, the government, upon the advice of the Food and Nutrition Board of the National Research Council and the Council of Foods and Nutrition of the American Medical Association, adopted a program of enriching white flour with synthetic thiamine, riboflavin, niacin and iron. The addition of calcium was optional. In January 1943, Food Distribution Order No. 1 required the enrichment of all white bread produced by commercial bakers. To insure continuity of the enrichment program, most of the states have passed laws requiring the enrichment of flour within their borders.

The philosophy of the enrichment program has been summarized as follows: (*a*) It is immediate and direct and brings into the diet of those consuming enriched bread, the dietary supplements which they need most, so far as this is indicated by the present knowledge of nutrition and of dietary deficiencies. The cost is very small. Enriched flour will supply close to one-half of the daily requirements of thiamin, riboflavin, niacin and iron and the cost should not exceed about thirty cents per person per year. (*b*) The program is not one of restoration of the dietary accessories removed in milling but rather it is directed toward the supplementation of the diet at those points and with those materials which are desirable in added amounts as disclosed in nutrition surveys. (*c*) It does not disturb or alter the normal practices in the manufacture of flour and bread. (*d*) It does not impair the storage behaviour of flour.

Table II shows the standard of identity for enriched flour and, for purposes of comparison, the vitamin and iron contents of whole wheat and of Canada Approved Vitamin B white flour.

In Canada, the first philosophy was adopted. Because whole wheat would

TABLE II

COMPARISON OF FLOURS

Nutrient	Enriched	Whole Wheat	Canada Approved
Thiamin	2.0- 2.5 mgms./lb.	2.25 mgms./lb.	1.2 mgms./lb.
Riboflavin	1.2- 1.5	0.5	0.2
Niacin	16.0- 20.0	25.0	4.0
Iron	12.0- 16.5	17.0	3.0

not meet consumer approval, it was hoped that a flour of longer extraction; that is, containing more of the outer layers of the wheat kernel; could be manufactured which would be richer in vitamins and minerals and yet be labelled white flour. A Canadian Order in Council P.C. 489 (Jan. 22, 1942) was adopted which introduced specifications for the manufacture of a new type of flour. It was to contain not less than 400 I.U. of thiamine per pound (1.2 mg. per lb.) with the other members of the vitamin B complex in the quantities associated with this amount of vitamin B_1 in the wheat from which the flour was produced. This flour was to be called Vitamin B White Flour, Canada Approved. At the same time, the enrichment of flour with synthetic vitamins was forbidden and declared an adulteration of flour. At the outset of the program, the government encouraged the use of Canada Approved flour and the baking industry conducted an extensive advertising campaign. However, within a few weeks, the sales of Canada Approved flour dropped to a low level (around 7% although the Army in Canada used only this flour) and have never recovered. The present consumption of Canada Approved flour is under 3% of all sales of flour in Canada.

In January 1943, at a conference of millers, bakers, nutritionists and government officials, Tisdall stated that, according to the available evidence, the national diet was definitely deficient in thiamine and riboflavin and probably in niacin, and there was no use in making Canada Approved flour that people will not buy and, in any case, this flour could do nothing to relieve the riboflavin deficiency. He agreed with the millers that the only sound procedure was to make an acceptible flour as high as possible in natural vitamins and to use that flour as a carrier for the needed mineral elements and synthetic vitamins.

In Newfoundland, as the result of the nutritional study reported above, the government in June 1944, required that all flour imported into Newfoundland must be enriched at the levels now employed in the United States.

CONCLUSION

In conclusion, it appears that nutritional deficiencies are widespread in Canada, the United States and Newfoundland. In the United States and Newfoundland, the governments have adopted programs of enriching white flour with essential vitamins and iron to such an extent as to supply one-half the daily optimum requirements of these essentials, together with an educational and economic program to improve the quality of the daily diet. In Canada, the government has attempted to improve the quality of the daily diet chiefly

by education together with promotion of a longer extraction flour which has not met consumer acceptance and which, even if it had, would not supply appreciably more of the vitamins than the previous white flour. Therefore, the practitioner in Canada should not be lulled into a false sense of security regarding the nutritional quality of the Canadian diet. There is no reason to suppose that malnutrition is rare.

REFERENCES

(1) Dunlap, F. L.: *White Versus Brown Flour.* Wallace and Tiernan Co. Inc.

(2) Ebbs, J. H.: Nutritive requirements in pregnancy and lactation, in *Handbook on Nutrition.* American Medical Association, Chicago, 1943

(3) Ebbs, J. H., Tisdall, F. F. and Scott, W. A.: The influence of prenatal diet on the mother and child. J. Nutrit. **22**, 515-526 (1941)

(4) Final report of the New York State Joint Legislative Committee on Nutrition: *Meals for Millions*, 1947

(5) Jolliffe, N, McLester, J. S. and Sherman, H. C.: The prevalence of malnutrition. J. Amer. Med. Assn. **118**, 944-950 (1942)

(6) Kruse, H. D.: A concept of the deficiency states. Millbank Memorial Fund Quarterly **20**, 245 (1942)

(7) Macy-Hoobler, I, and Williams, H. H.: *Hidden Hunger.* The Jacques Cattell Press. 1945

(8) Mott, F. D. and Roemer, M. I.: *Rural Health and Medical Care.* McGraw-Hill Book Company Inc., 1945

(9) Nutrition in Newfoundland. J. Canad. Med. Assn. **52**, 227-250 (1945)

(10) Pett, L. B.: Are there nutritional problems in Canada? J. Canad. Med. Assn. **59**, 326-328 (1948)

(11) Pett. L. B. and Hanley, F. W.: Nutrition survey on a Nova Scotian Island. J. Canad. Med. Assn. **59**, 230-236 (1948)

(12) Robertson, E. C. and Galloway, M. E.: Vitamin C Content of Diets of Lower Income Toronto Families. J. Canad. Med. Assn. **59**, 236-240 (1948)

(13) United Nations Conference on Food and Agriculture, Hot Springs, Va., *Final Act (and Section Reports)*, 1943.

(14) Wohl, M. G.: *Dietotherapy.* W. B. Saunders Company, Philadelphia, 1945.

(15) Woodbury, R. M.: *Food Consumption and Dietary Surveys in the Americas.* Report by International Labour Office to the Eleventh Pan-American Sanitary Conference held in Rio de Janeiro, Sepr. 7-18, 1942.

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EDITORIAL

THE FLOOD TIDE

"There is a tide in the affairs of men,
Which, taken at the flood, leads on to fortune;
Omitted, all the voyage of their life
Is bound in shallows and in miseries.
On such a full sea are we now afloat;
And we must take the current when it serves,
Or lose our ventures."

—*Shakespeare.*

It would be especially appropriate for every student of medicine, whether so-termed premedical or medical, as a future member of the medical profession, to ponder the above speech of Brutus to Cassius while he was discussing their future course of action.

As Osler has pointed out, the medical profession has four great "features": a noble ancestry, a remarkable solidarity, a progressive character, and a singular beneficence. It behooves each student of medicine to appreciate these features of his chosen profession and to realize that presently, it will be his individual responsibility to maintain and to advance each of them, and now, therefore, at the beginning of a new year, while he is still a student, he should evaluate his personal ideals and objectives and critically assess the present trends in medical practice and in health services in general.

Each student and each practitioner of medicine must have his personal ideals and goals in life and do his utmost to realize and to achieve them. True, not all in the medical profession live up to the highest ideals, far from it, they are only human, but they have ideals, which mean much, and those ideals are realizable, which means more. Each should set for himself high, unselfish ideals and strive to attain them. "To

have striven, to have made an effort, to have been true to certain ideals—these alone are worth the struggle." Consider well the words of Sir William Osler in an address (*The Master-word in Medicine*) which he gave to the medical students here, at the University of Toronto, forty-five years ago:

"A conscientious pursuit of Plato's ideal perfection may teach you the three great lessons of life. *You may learn to consume your own smoke.* The atmosphere is darkened by the murmurings and whimperings of men and women over the non-essentials, the trifles that are inevitably incident to the hurly burly of the day's routine. Things cannot always go your way. Learn to accept in silence the minor aggravations, cultivate the gift of taciturity and consume your own smoke with an extra draught of hard work, so that those about you may not be annoyed with the dust and soot of your complaints.

More than any other the practitioner of medicine may illustrate the second great lesson, *that we are here not to get all we can out of life for ourselves, but to try to make the lives of others happier.* This is the essence of that oft-repeated admonition of Christ, "He that findeth his life shall lose it, and he that loseth his life for my sake shall find it," on which hard saying if the children of this generation would only lay hold, there would be less misery and discontent in the world. It is not possible for anyone to have better opportunities to live this lesson than you will enjoy. The practice of medicine is an art, not a trade; a calling, not a business; a calling in which your heart will be exercised equally with your head. . . .

And the third lesson you may learn is the hardest of all—*that the law of the higher life is only fulfilled by love, that is charity.* Many a physician whose daily work is a daily round of beneficence will say hard things and think hard thoughts of a colleague. No sin will so easily beset you as uncharitableness toward your brother practitioner. . . . From the day you begin practice never under any circumstance listen to a tale told to the detriment of a brother practitioner. And when any trouble or dispute does arise, go frankly, ere sunset, and talk the matter over, in which way you may gain a brother and a friend. Very easy to carry out, you may think! Far from it, there is no harder battle to fight. . . ."

"To each one of you the practice of medicine will be very much as you make it—to one a worry, a care, a perpetual annoyance; to another, a daily joy and a life of as much happiness and usefulness as can well fall to the lot of man, because it is a life of self-sacrifice and of countless opportunities to comfort and help the weak-hearted, and to raise up those that fall. In the student's spirit you can best fulfill the high mission of our noble calling—in his *humility*, conscious of weakness, while seeking strength; in his *confidence*, knowing the power while recognizing the limitations of his art; in his *pride* in the glorious heritage from which the greatest gifts to man have been derived; and in his sure and certain *hope* that the future holds for us still richer blessings than the past." (Osler, in *The Student Life.*)

Now, during your student days, the tide is at the flood. As future members of the medical profession, ponder deeply. Take the current while it serves, or lose your venture.

HUMANISM AND MEDICINE

H. B. VAN WYCK[1]

PART IV

THE GREAT AGE OF GREECE
490 - 332 B.C.

THIS PERIOD—one of the most important centuries-and-a-half in history—was a noble setting for the world's first great physician—Hippocrates of Cos. The appearance at this time of abundant genius tempts the recorder to an enthusiasm and wonder which must not fail to strike a vibrant chord in the impressionable reader who can thrill to beauty and wisdom and wonder at its creation. In the Greek world and especially in the Athens of Pericles, the historian finds a greater concentration of creative intellects of the highest order than in any comparable time and place in the records of man.

To the western European, those lands that border on the Mediterranean should represent his spiritual birth place. From its shores, he has had a birth right of both science and humanism which has singled him out among the peoples of the world as chosen for high destiny; and, as his modern descendant surveys the past and beholds the achievements of these founders of his culture, the shores of that old sea, beside which all this took place, will never fail to provoke an intense and nostalgic interest. The Mediterranean coast line may well be more familiar to a Canadian than the shores of his Great Lakes beside which the events that took place are in comparison sparse and only locally significant. It is unfair to place emphasis on the contrast between the picturesque adventures of Champlain or La Salle and the campaigns of Hannibal, between the not unimpressive triumph of the railroader on the rock-bound coasts of Lake Superior and the formidable and still evident achievements of the Roman engineers or Greek architects. To the latter the centuries have added a significance and value that only great eras and crowded events could provide.

Each curve of the Mediterranean littoral revives in western man the memory of heroic deeds, tragic contests, the sacrifices of patriots, the creation of pristine beauty, or the early revelations of science. The Mediterranean was called by the ancients the centre of the earth and such it has been known through the centuries with the one fatuous exception in our time when an egregious and arrogant mountebank called it "Mare Nostrum." To western Europeans on both sides of the Atlantic, it is not only their sea but their intellectual and spiritual homeland; and should a hostile and despotic power grasp dominion over the waters that have carried time after time the defenders of western freedom, slavery may return to burden and submerge the democracies of the world. The centuries have drawn from its coasts a wealth of noble tradition and a legacy of philosophy, science and art for all mankind, and the return in spirit to

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survey the Mediterranean scene may well begin at the Greek world of the Fifth Century B.C., a century which began in earnest the provision of expanding horizons for posterity.

Nature provided a precious setting for these gifted Greeks. The homeland was the Greek Peninsula, the Islands of the Aegean, and the neighbouring coast of Asia Minor. This area, crossed by the two great mountain arcs of Europe, the Dinaric and the Alpine, subject in geological ages to frequent earthquake and the outpouring of the glassy lava known to the ancients as the commercially useful obsidian, and marked by festoons of submerged mountain tops in the Aegean islands of the archipelago, was, on the mainland of each continent, ribbed by fertile valleys running in clefts between the hills and mountains to countless harbors. These indent the colourful coastline and invited the adventurous and the often imperilled mariner to trade and safety. Everywhere the Greek of those early days could find beauty in his tree-clad hills, his vine-clad valleys and in the near distance his own harbour dotted with brave shipping from the many corners of his Mediterranean world. Commerce moved its wares by pack train, chariot wheel, sail, oar, or toil of the warfarer. Whatever he saw moving on his few roads or in the many water lanes was picturesque and often exotic; and, in his cities he saw the extravagant masonry of the East replaced by the chaste lines of temples whose symmetry and grace have remained the wonder of posterity. His vision was limited by the nearest mountain, but when he saw the sea, his unfettered fancy took easy flights to his colonial folk spread from Marseilles to the distant shores of the Black Sea. Thus divided into small valley and shore communities, the Greek people grew into a civilization of many independent city states; and, in the Fifth Century, suddenly flowered with a radiant bloom that no geographic or racial environment can explain except in Toynbee's words as a response to the challenge of danger. The challenge was danger of extermination and the challenger was the great despotic and military power of the adjacent Persian Empire.

With the defeat of despotism at Marathon, 490 B.C., began the Golden Age. Marathon could be called the first victory of the West over the East, of freedom and the spirit of free inquiry over slavery and the totalitarian idea. The mind of man began to shake free of its fetters. The victory was followed by an irresistible outbreak of national pride and the rapid advance of intellectual achievement was perhaps best explained as its natural result. The miracle of the Hellenic Age has a close analogy in England after the Armada. This great Age of Greece may be said to begin with Marathon and end with the fall of the Grecian mainland to the armies of Alexander in 332 B.C.—about a century-and-a-half during which Athens became a great naval power and the head of an empire—the Delian league. The centres of Greek intellectual activity were Athens, Corinth, Miletus, Syracuse and Thebes. Sparta contributed little except herself as the example of a state subordinated to military and despotic ends.

The Hellenic culture was preceded by the Cretan-Mycenean civilization which developed to its zenith about 1500 - 1200 B.C. among the inhabitants of the peninsula who were almost certainly Mediterranean in race. These left a tradition of a gloomy sacrificial religion

and the remains of their pottery and metal attest their skill as artificers. The ancestors of the Hellenes, however, were invaders from the north who came from the semi-arid grass lands of northern Russia. It has been customary to call these Aryan peoples, probably nordic and alpine in race, Achaeans and Dorians, who in their southern march displaced the Aeolians and Ionians, the latter fleeing across the seas to the coasts of Asia Minor, Sicily, the Black Sea and the tip of the Italian peninsula. By 600 B.C., Greek colonists had reached Massalia (Marseilles) and thus were the vanguard of civilization to our Western world.

Of statecraft, much was added to man's experience by these tiny communities and they served as examples of the trial of different methods of government about which histor|ans and philosophers could d|spute. But the priceless heritage they passed on to us was the beginning of physical science, and the free inquiry into the great questions of man's potential ends, the meaning of life, and the values of a moral universe. The incubus of superstition was unloaded and need never have burdened posterity again. All this was achieved by intellectual adventurers in science, mathematics, philosophy, ethics; and never since has creative art attained so quickly from primitive origins a nature of perfection.

The father of science was Thales of Miletus, and he was followed by a brilliant band of inquiring thinkers who began to lay aside the dead weight of superstition and interpret the physical world by means of a free intellect. The social and political pattern of life in the small city state promoted freedom of speech, intellectual discussion, self-expression, and freedom of thought; and these essential means to progress are the Greek's great gift to posterity; a legacy from which the western European world has had great profit. This sudden unshakling of the human mind took place among a people whose priestly caste, at no time powerful, never succeeded in establishing over these communities the sacerdotal tyranny of Babylon or the clerical suppression of free inquiry which was to delay the progress of western Christendom for a millenium. Of the Greek of those days, the cosmopolitan spirit engendered by his roving, restless, adventurous, and colonizing life was congenial to the full advance of the mind; and he who goes abroad and feels the impact of new ideas and alien customs, will early learn to replace thoughtful credulity by a more fruitful and critical skepticism. The first problem of the Greek intellect was to explain nature and human experience in terms of reason rather than supernaturalism. As yet philosophy and science were undifferentiated; and these early thinkers attempted to explain the nature of the universe in physical terms. The catalogue of these early philosopher scientists of the "cosmological" period of philosophy is weighted with a galaxy of brilliant intellects—and their crude efforts to solve the eternal riddles by materialistic hypotheses and empirical observation marked a far advance from the primitive and naive faith in supernaturalism of the earlier peoples.

Thales, the father of science, was born at Miletus (640 B.C.), and began his education by studying in Egypt. He rapidly passed from the concrete problems of land surveying to abstract concepts of the geometry of lines. Thus was a new science born. The Egyptian whose major problem was the sorting out of fields after the annual mundation

of the Nile Valley, had never produced the abstract theorems which Thales announced. That a circle is bisected by its diameter, that angles at the base of an isocoles triangle are equal, and that the angle in a semi-circle is a right angle—such basic formulae, almost self-evident to us, were tremendous discoveries to the contemporary world. He taught the Egyptians how to measure the height of the pyramids and to his fellow citizens in Miletus he predicted with accuracy an eclipse, and measured the diameter of the Sun. In an effort to find a unifying concept of the universe, Thales proposed that water underlay all reality, a rather childish absurdity. Nevertheless the mere attempt at a cosmic metaphysics was a portent of progress and the absurdity is lessened by the reflection that Thales lived in an Aegean world where there was much more water than land.

Others of the Milesian School were Anaximander and Anaximanes. Each made a choice of the primary element—the former choosing "chaos" and the latter "air". The Eleatic School in the Italian peninsula — Xenophanes, Parmendides and Zeno followed the trail of the Milesians and were the first to distinguish a noble monotheism from the cruder anthropomorphic and animistc cults. Xenophanes' statement on man's search for truth has a modern ring and reveals that the Hebrews of that period did not alone possess religious insight. "There never was nor ever will be any man who knows with certainty the things about the gods and about all things. For even if he does happen to get most things right, still he himself does not know it. Mere opinions, however, all may have."

Pythagoras of Crotona (born in Samos 582 B.C.), was perhaps the most famous and influential of these ancient sages. He visited Egypt and Babylonia in search of mathematics and founded his views on the relations of numbers. This has conferred on him the doubtful honour of being the patron saint of every crackpot who dabbles in astrology, numerology, or pyramid mensuration. He returned to Greece, formed a brotherhood, and became an immortal. Based on the numerical relationship of the vibrations of the harmonious tones of strings to their length, the Pythagorean assumption that mathematical formulae govern the world of nature, gave a directive stimulus to the advance of natural science. The generative impulse that love of abstract thought gives to practical science is proved by the advance made by the Pythagorean School in mathematics and the application by Archytas, a friend of Plato, of geometry to mechanics. Pythagoras improved the geometry of his day and united it with arithmetic. His best remembered theorem is the relation of the square of the hypothenuse of a right angle triangle to the squares of the other sides. He taught that the moon was lighted by reflection, that the world wasn't flat and did not stand still, and identified the evening star. Pythagoras lives in the influence he exerted on his Greek disciples and is held in reverence by all those who listen for the "music of the spheres."

Democritus of Abdera in Thrace (460 B.C.) followed the usual pattern of these earlier philosophers by extensive travel throughout the ancient world of the Near East. The legend of the visit of Hippocrates, who was called to attend the "Laughing Philosopher" as Democritus was known to his townsmen, excites the imagination. Hippocrates, who came to certify insanity, remained

to wonder at the sublime cosmic guess of his patient; for Democritus proposed the hypothesis of the atomic structure of the universe—a brilliant intuitive prophesy of the more precise definitions of modern chemistry. This first among the philosophic materialists left lofty moral precepts and thus ennobled the Epicurean religion which followed his teaching; and the doctrine that our immortality consists in the undestructibility of the atom, was balanced in the moral scale by the tenet that the moral character is determined not by a man's acts but by his will.

Others of these "cosmologists" were Heracleitus (500 B.C.) who held that "change" and Parmenides that "being not becoming" were the fundamental realities, whereas Empedocles (470 B.C.) attempted a pluralistic explanation which subsequently became the basis of the Hippocratean humoral theory. With Anaxagoras (500 B.C.) the first philosopher to choose Athens as his abode and to foreshadow the evolutionary idea of differentiation out of chaos, the cosmological period of Greek science and philosophy came to an end.

What may be termed the anthopological period began with the passing of the Persian shadow. Athens became the centre of the new thought; and, with Socrates as its first exponent, the study of the Universe in physical terms gave way to the study of man and his political and social environment in the state. Parallel with these unprecedented flights of the human mind, modern medicine had its first conscious beginning.

RECENT ACCESSIONS TO THE MEDICAL READING ROOM

Annual review of microbiology, Vol. 2. 1948.
Anonymus Londinensis: **The medical writings of Anonymus Londinensis.** 1947.
Baruch Committee on Physical Medicine: **Report on a community rehabilitation service and center.** 1947.
Beckman, H.: **Treatment in general practice,** ed. 6. 1948.
Bergey, D. W.: **Manual of determinative bacteriology,** ed. 6. 1948.
Colson, J. H. C.: **The rehabilitation of the injured,** Vol. 2: **Remedial gymnastics.** 1947.
Coward, K. H.: **The biological standardisation of the vitamins,** ed. 2. 1947.
Dunlap, F. L.: **White versus brown flour.** 1945.
Goldberger, E.: **Unipolar lead cardiography.** 1947.
Johnson, W. M.: **Years after fifty.** 1947.
Marcus, J. R.: **Communal sick-care in the German ghetto.** 1947.
Meredith, W. J. (Ed.): **Radium dosage; the Manchester system.** 1947.
Millin, T.: **Retropubic uninary surgery.** 1947.
Mott, F. D. and Roemer, M. I.: **Rural health and medical care.** 1948.
National Foundation for Infantile Paralysis: **Collected reprints of the Grantees of the National Foundation.** (1947).
Palmer, A. M.: **Medical patents.** 1948.
Physical Society of London, Colour Group: **Report on defective colour vision in industry.** (1946).
Rockefeller Foundation, International Health Division: **A survey of the epidemiological services in Canada.** 1948.
Saul, L. J.: **Emotional maturity.** 1948.
U. S. Social Security Administration: **Need for medical care insurance.** 1946.
White, C. S. and Weinstein, J. J.: **Blood derivatives and substitutes.** 1947.
Willard, H. H.: **Instrumental methods of analysis.** 1947.
Willard, H. S. and Spackman, C. S.: **Occupational therapy.** 1947.

ABSTRACTS

BIOCHEMISTRY

Platelet Extracts, Fibrin Formation and Interaction of Purified Prothrombin and Thromboplastin. A. G. Ware, J. L. Fahey and W. W. Seegers: Amer. J. Physiol. **154**, 140-147 (July 1948).

The authors have evolved a theory far more complex than the generally accepted, over-simplified conception of the mechanism of blood clotting which regards the role of the blood platelets in accelerating blood coagulation as being to supply thromboplastin. Quick *et al.* have suggested that the platelets provide an activator of inactive thromboplastin, but only very little thromboplastin. The authors confirmed the low thromboplastin content of platelets and demonstrated the presence of two other substances: Platelet Factor 1 which catalyzes the change of prothrombin to thrombin by thromboplastin and calcium ions, acting like serum Ac-globulin; and Platelet Factor 2 which hastens the action of thrombin on fibrinogen, acting like acacia and some other colloids. Early investigators probably mistook these accelerators for thromboplastin.

Serum Ac-globulin increases the rate of thrombin formation using purified prothrombin, thromboplastin and calcium ions. Plasma Ac-globulin acts more slowly because it is the precursor of serum Ac-globulin and forms the latter when acted upon by thrombin. Platelet Factor 1 has an accelerator activity quantitatively identical with that of serum Ac-globulin but it is far more thermo-stable. Therefore it appears that these two accelerators are different proteins. Platelet Factor 2 decreases the time for clot formation when in mixtures of thrombin and fibrinogen, when the plasma is used in high enough concentrations. This factor also forms a coagulum with thrombin, the precursor of which is not known and is not fibrinogen.

Correlating these new facts, the authors postulate the following reactions in blood clotting: (1) thromboplastin from platelets or tissue acts on plasma prothrombin to form a small amount of thrombin, catalyzed by platelet accelerator and calcium ions; (2) plasma Ac-globulin is activated by this thrombin to form serum Ac-globulin which becomes the main accelerator in the formation of thrombin; and (3) thrombin activates fibrinogen to form fibrin.

A. Bernstein

MEDICINE

Lysozyme Activity in Ulcerative Alimentary Disease. Meyer, Gellhorn, Prudden, Lehman and Steinberg: Am. J. Med. **5**, 482-502 (Oct. 1948).

Lysozyme, a bacteriolytic, mucolytic enzyme present in nasal secretions, saliva, tears and egg-white has been found in the gastro-intestinal mucosa of animals and man. Several experimental and clinical observations point to it as an etiological factor in peptic ulcer, regional enteritis and chronic ulcerative colitis. A marked increase in lysozyme concentration has been found in alimentary ulcerative disease, whereas a fall in the enzyme titres accompanies clinical improvement. The reason for localized overproduction of the enzyme is obscure. Following oral administration, crystalline lysozyme produces ulcerative lesions and removes surface mucus. It is suggested that lysozyme denudes the surface of protective mucus, permitting necrosis by proteolytic enzymes, presumably furnished by micro-organisms. Although circumstantial, the evidence presented is impressive, especially with regard to chronic ulcerative colitis.

G. L. Ralph

Longevity in Rheumatic Fever. M. G. Wilson and R. Lubschez: J.A.M.A. **138**, 794-798 (Nov. 1948).

Rheumatic fever is recognized as an important cause of death in persons under 20 years of age. It is of greater importance to know the prospects of an afflicted child surviving childhood and puberty and reaching adulthood. 1,042 such children were followed over a period of thirty years from 1916 to 1947, and a life-table constructed to estimate the chance of survival of these children. It was observed that the chance of an affected child surviving for 15 years after the onset of the disease is 4 in 5; 20 years, 3 in 4; and 30 years, 2 in 3. The overall chance to survive to the age of 40 years is 1 in 2. The highest mortality rate occurred 1 year after onset, the greatest risk was at puberty irrespective of age at time of onset and there was no significant sex difference in the age-specific mortality rates. At last observation, 90% of the patients between 21 and 42 years of age were able to carry on their normal activities without circulatory symptoms. During the past 20 years,

there has been no significant change in the mortality rate from rheumatic fever. The causes of death and the incidence of different lesions in this disease are also reviewed.

H. R. Rowsell

PATHOLOGY

Coarctation of the Aorta and the Aortic Isthmuses. J. L. Bremer: Arch. Path. **45**, 425-434 (Apr. 1948).

The author presents Bonnet's classification of coarctation of the aorta: (1) newborn type, in which narrowing of the aorta occurs between the origin of the left subclavian artery and the distal end of the ductus arteriosus, this segment is commonly termed the aortic isthmus; and (2) adult type, in which the narrowing of the aorta is always in the immediate vicinity of the distal end of the ductus arteriosus appearing "as if the aorta had been constricted by a ligature."

The pathogenesis of coarctation is discussed. The adult form is commonly ascribed to an extension of the obliterative process in the ductus arteriosus to the aortic wall with resultant narrowing of the lumen. Two older theories of the cause of the newborn type are presented. One theory claims the narrowing is due to a failure of the aortic arch to expand with the increased blood flow through it after birth. A second theory explains the widening of the aorta beyond the aortic isthmus as due to kinking in a sharply angled aortic arch.

The author describes his own theory of the pathogenesis of coarctation of the newborn type. Relating the two forms of coarctation, he traces the embryological development of the oartic arch. The primitive left dorsal aorta joins the fourth branchial arch at the site of the aortic isthmus. Obliteration of this primitive vessel proceeds in a manner similar to that occurring in the ductus arteriosus after birth and extension of the process into the wall of the left fourth branchial arch may be the cause of coarctation of the newborn type.

D. I. Gove

NEUROLOGY

Management of Paralyzed Bladder. G. Baumrucker: Arch. Surg. **56**, 484-507 (Apr. 1948).

The author discusses the treatment of patients with injuries of the spinal cord and resultant paralysis of the bladder. The aim of therapy is the development of an automatic bladder. Most patients had either an initial suprapubic drainage, with the catheter placed high in the bladder to avoid fibrosis in the bladder neck, or urethral catheterization, both with frequent cleansing and irrigation. The latter was provided by (1) a closed system manually controlled, or (2) a tidal irrigator using isotonic saline. A small Foley retention catheter was always used. These methods tended to develop tone in the flaccid bladder and relaxation in the spastic one. The author found that a cystometric pressure of over 35 mm. Hg was satisfactory for automaticity and to develop this, he used training of the muscles of the abdomen as well as of the bladder. Fibrosis of the bladder neck, infection and calculus formation must always be guarded against by X-ray examination, irrigation and drug therapy, combined with early ambulation, exercise and adequate diet.

His results with 38 patients showed that 32 developed automaticity; of the failures, 5 had quadriplegia with a flaccid abdomen and one is still undergoing reconstructive surgery. The author advocates individual attention and training, early exercise and rehabilitation in the readjustment of these patients.

Miss A. I. Scott

OBSTETRICS

Early Rising After Delivery. E. L. Cornell, and J. J. Mullen: Amer. J. Obstet. & Gynecol. **55**, 768 (May 1948).

The authors report on one thousand patients admitted to Henrotin Hospital for delivery representing a typical cross section of postpartum cases. The patients were allowed up on the sixth day or earlier (80% before the fifth day). At the time of discharge, they were in a better condition than if they had remained in bed eight or more days. They were able to adapt themselves more readily to their daily household routine. Maternal morbidity and episiotomy wound healing were not adversely affected. None of those delivered vaginally developed thrombophlebitis, suggesting a tendency toward a reduction of this complication. There was no case of uterine prolapse. The rate of uterine involution was increased. When necessary, owing to overcrowding, the patient could be discharged earlier than heretofore with a greater margin of safety. The postoperative

course of the fifty-three cases of cesarian section included in the group was more nearly uneventful. Distention was infrequent. The necessity for enemas and catheterization was lessened when the patient was permitted bathroom privileges on the first postoperative day. One case developed thrombophlebitis on the thirtieth postoperative day.

W. G. B. Casselman

PSYCHIATRY

Psychiatry in the General Hospital. Keyes, Bookhammer and Kaplan: Am. J. Psychiatry, **105**, 90-95 (Aug. 1948).

At the Jefferson Medical Hospital, there has been an increase in the allotment of time, space and personnel to out-patient psychiatric services. The goal is a psychiatric ward service as an integral part of the hospital. In 1941 and 1946, 50% of the psychiatric consultations were for psychosomatic disorders such as essential hypertension, peptic ulcer, asthma, thyrotoxicosis, while 27 - 32% were for psychoneuroses, chiefly the anxiety and conversion hysterias. The necessity for a psychiatric ward service in a general hospital and its mode of function are stressed.

A. C. Parkin

Intelligence and Emotional Instability. J. G. Dewan: Am. J. Psychiat. **104**, 548-554 (Feb. 1948).

This study was done on all recruits, with the exception of those known to have been in a mental hospital, who passed through an induction centre over a 15-month period. The estimation of mental retardation was based on clinical judgment with test results aiding in a subsidiary capacity. Emotional instability was diagnosed on the basis of history, general be haviour and response to conversational questioning. Of those diagnosed as mentally retarded, 47.7% were considered emotionally unstable while only 19.7% of the non-retarded recruits were diagnosed unstable. The evidence suggests that the incidence of psychoneurosis and other patterns of emotional instability declines as the degree of intelligence advances although this becomes much less evident in the upper ranges of intelligence. Possible factors responsible for this association are discussed.

A. C. Parkin

PSYCHOLOGY

College Grades and the Group Rorschach. G. M. Thompson: J. App. Psychol. **32** (Aug. 1948).

The lack of a perfect correlation between college grades and intelligence, as currently measured, is probably, in part, due to imperfections in the measurement of intelligence as well as to the unreliability of the criteria employed. Yet, to a greater degree, it is an indication that other factors beside sheer academic ability are of considerable importance in evaluating any single student's academic success. The measurement of personality factors, therefore, seems to be of paramount importance to present-day education in its guidance, grouping and admission programs. A measurement of non-intellectual factors is unfortunately not yet available to the ordinary tester who continues to rely on the easily obtained aptitude scores.

A promising technique now being employed to measure the adjustment aspects of academic success is the Group Rorschach, which has already been used to advantage on a large scale by Ruth Monroe and her colleagues at Sarah Lawrence College, where it is now a standard entrance procedure. It is reported that the Inspection Rorschach (an abbreviated check list to be used by examiners well acquainted with the test) was associated with grades to a somewhat higher degree than the A.C.E. Psychological Examination, one of the most widely used tests at the college level. Whereas the A.C.E. was more successful in predicting success, the Rorschach succeeded better in predicting academic failure.

The Rorschach test can be quantified and still retain diagnostic value. The time of administration is one hour for a group and the subjective elements are minimized in the scoring by adherence to a pre-determined set of categories. It would appear that the Group Rorschach can be used in the prediction of academic success above and beyond that offered by a standardized intelligence test.

W. E. Sullivan

SURGERY

Sulpha Granuloma — A New Pathological Entity. T. H. Williams: D.V.A. Treatment Service Bull. **3**, 5-9 (July 1948).

It has become common surgical practice to dust a powdered sulphonamide into surgical

wounds where infection is threatening or has occurred. Surgically, results appear to be good in most cases. However, many wounds subsequently develop tender areas and frequently discharge from sinus openings. On investigation, granulation tissue has been found containing a foreign body granuloma formation of the reticulo-endothelial type without caseation but with crystalline inclusions in giant cells. The insolubility of the sulpha powder in tissues of some patients has been brought to the attention of surgeons.

Sulpha powder dusted in wounds does not always produce a granulomatous reaction. Nevertheless, in an appreciable number of cases, it remains as unabsorbed foreign material provoking a granulomatous tissue reaction. Similar reactions have been noted in kaolin granulomata of intestinal mucosa.

The author lists literature in which surveys show the local application of sulpha drugs in burns, wounds and fractures produces little beneficial reaction; rather it may be harmful due to the chronic granuloma which may result.

F. Williamson

The Traumatic Conditions of the Abdomen. Metz, Householder and Dangremond: Am. J. Surg. **76**, 368-377 (Oct. 1948).

The authors point out that injury to intra-abdominal organs is not uncommon and is usually serious. Successful management depends upon early, accurate diagnosis and immediate, intelligent treatment. The article begins with a general discussion of the anatomy, types of injury, mode of examination and treatment of abdominal trauma. The causes, clinical findings, diagnosis and management of injuries to the liver, gall bladder, spleen, pancreas, kidney, stomach, intestine, mesentery, blood vessels, urinary bladder and urethra are simply, concisely and individually dealt with throughout the rest of the paper. The original text is well worth reading in its entirety.

G. L. Ralph

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*REFERENCE: Marie Wessels, M.D. Human Fertility, Vol. 5, No. 6, December, 1940.

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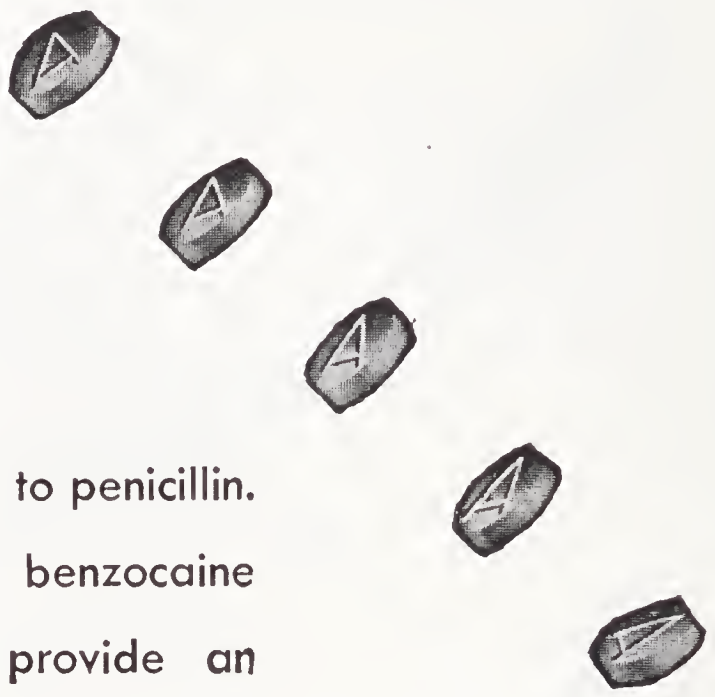

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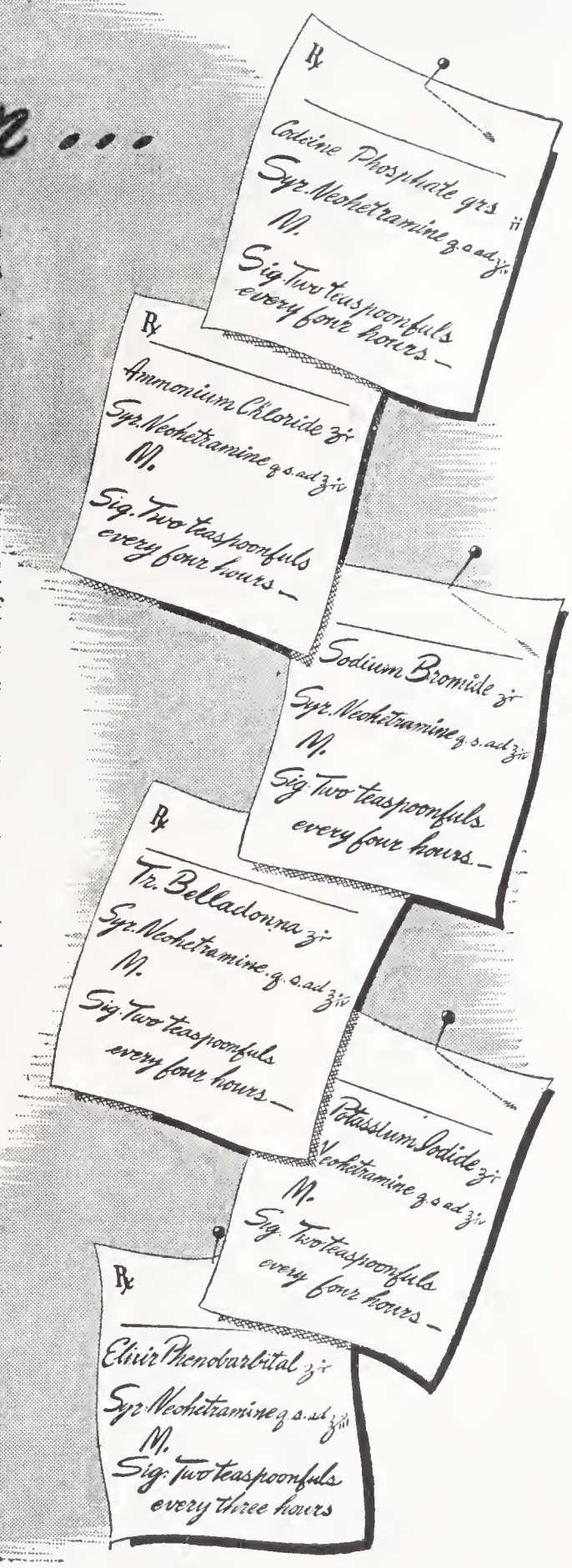

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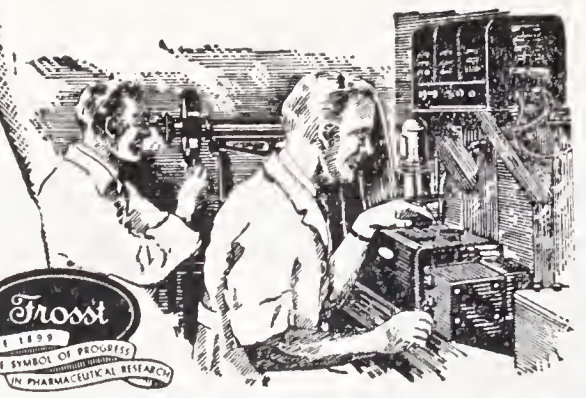

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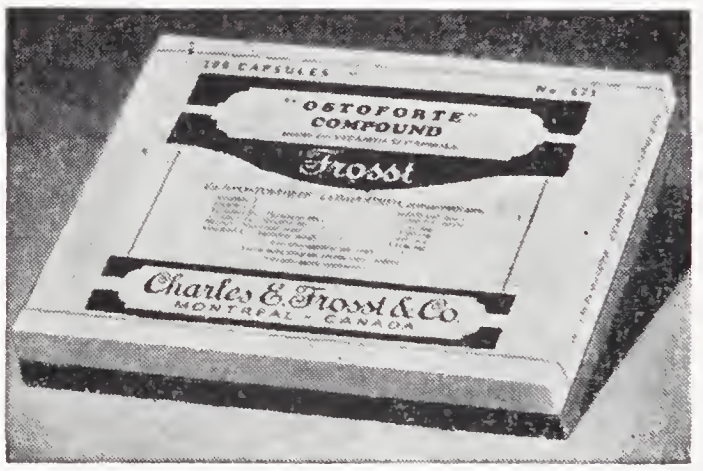

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